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<p>(21) International Application Number: PCT/KR98/00268</p> <p>(22) International Filing Date: 31 August 1998 (31.08.98)</p> <p>(30) Priority Data: 1997/46769 11 September 1997 (11.09.97) KR</p> <p>(71) Applicant (for all designated States except US): YUHAN CORPORATION [KR/KR]; #49-6, Taebang-dong, Tongjak-ku, Seoul 156-020 (KR).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): LEE, Bong, Yong [KR/KR]; Dongsin Apt. #109-1406, Jungja-dong, Janggan-ku, Suwon-si, Kyonggi-do 440-301 (KR). KIM, Jae, Gyu [KR/KR]; Hyangchon Apt. #103-2503, 899-7, Pyungchon-dong, Dongan-ku, Anyang-si, Kyonggi-do 431-070 (KR). BHANG, Kee, Hoon [KR/KR]; #302, 1002-14, Hokye-1-dong, Dongan-ku, Anyang-si, Kyonggi-do 431-081 (KR). SIM, Woo, Jeon [KR/KR]; Hanmaroo Apt. #110-1304, Dunsan-dong, Su-ku, Taejeon 302-173 (KR). HWANG, Hyun, Jun [KR/KR]; #8/3, 1-208, Bongchon-3-dong, Kwanak-ku, Seoul 151-053 (KR). PARK, Yoo, Hoi [KR/KR]; Fine Apt. #105-803, 692, Sambang-dong, Kimhae-shi, Kyongsangnam-do 621-190 (KR). HWANG, Soon, Ho [KR/KR]; #183-1,</p>		<p>Hwasu-dong, Jangan-ku, Suwon-si, Kyonggi-do 440-150 (KR). JUNG, Young, Hwan [KR/KR]; Chugong Apt. #622-407, Byulyang-dong, Kwachun-si, Kyonggi-do 427-040 (KR). YI, Won, Hui [KR/KR]; Dongyang Apt. #1-513, Hokye-3-dong, Dongan-ku, Anyang-si, Kyonggi-do 431-083 (KR). SHIM, Jae, Young [KR/KR]; Samik Apt. #110-1302, Kumkwang-dong, Sungnam-si, Kyonggi-do 462-241 (KR).</p> <p>(74) Agents: CHOI, Kyu, Pal et al.; 824-20, Yeoksam-dong, Kangnam-ku, Seoul 135-080 (KR).</p> <p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p>Published With international search report.</p>
<p>(54) Title: THIOUREA DERIVATIVES OR NON-TOXIC SALTS THEREOF FOR INHIBITING RAS-TRANSFORMED CELL GROWTH</p> <div style="text-align: center;"> <p>(I)</p> </div>		
<p>(57) Abstract</p> <p>The present invention relates to novel thiourea derivatives of formula (I) which possess an excellent activity for inhibiting ras-transformed cell growth, pharmaceutically acceptable salt or stereoisomer thereof, wherein R₁ represents hydrogen; straight-chain or branched C₁-C₈-alkyl which is optionally substituted by substituents selected from a group consisting of halogen, C₁-C₆-alkoxy, C₁-C₆-alkoxycarbonyl and di(C₁-C₄-alkyl)amino; C₂-C₆-alkenyl; C₁-C₄-alkoxycarbonyl; C₃-C₆-cycloalkyl; phenyl which is optionally mono- to trisubstituted by substituents selected from a group consisting of halogen, C₁-C₆-alkyl, C₁-C₆-alkoxy, C₁-C₆-alkylthio, halogeno-C₁-C₆-alkyl, azido, nitro, amino, phenyl, di(C₁-C₄-alkyl)amino and hydroxy; phenyl-C₁-C₄-alkyl; naphthyl which is optionally substituted by di(C₁-C₄-alkyl)amino; benzoyl; pyridyl which is optionally substituted by substituents selected from a group consisting of halogen and C₁-C₆-alkoxy; or adamantyl; R₂ and R₃ independently of one another represent hydrogen, straight-chain or branched C₁-C₆-alkyl, C₃-C₆-cycloalkyl or benzyloxybenzyl; R₄ represents C₁-C₄-alkyl substituted by phenyl wherein the phenyl moiety is optionally mono- to trisubstituted by substituents selected from a group consisting of halogen, halogeno-C₁-C₄-alkyl, C₁-C₄-alkylenedioxy, C₁-C₆-alkyl, nitro, C₁-C₆-alkoxy, carboxyl and C₁-C₆-alkoxycarbonyl; naphthyl-C₁-C₄-alkyl; thiophenyl-C₁-C₄-alkyl; C₁-C₆-alkyl which is optionally substituted by substituents selected from a group consisting of pyridyl, oxypyridyl, C₁-C₆-alkoxy and C₁-C₆-alkylthio; or C₂-C₆-alkynyl; and X represents nitro or cyano. The present invention also relates to a process for the preparation of the thiourea derivatives and a pharmaceutical composition for inhibition of ras-transformed cell growth comprising the same as an active ingredient.</p>		

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THIOUREA DERIVATIVES OR NON-TOXIC SALTS THEREOF FOR INHIBITING RAS-TRANSFORMED CELL GROWTH

TECHNICAL FIELD

The present invention relates to novel thiourea derivatives, pharmaceutically acceptable non-toxic salts or stereoisomers thereof which possess an excellent activity for inhibiting ras-transformed cell growth. The present invention also relates to a process for the preparation of the thiourea derivatives and a pharmaceutical composition for inhibition of ras-transformed cell growth comprising the same as an active ingredient.

BACKGROUND ART

A ras protein is farnesylated or geranylgeranylated by farnesyltransferases [farnesyl protein transferase (hereinafter referred to as "FPTase") or geranylgeranyl protein transferase (hereinafter referred to as "GGPTase"), respectively] to be translocated into an intracellular membrane, in which the ras protein is activated or inactivated by GTP or GDP. The activated ras protein forwards the downstream signal transduction pathways to transmit the outside signal into nucleus. And then, the nucleus activates translational factors (e.g., myc, jun, fos etc.) to forward cell growth or nucleus division. (M. Barbacid, Annu. Rev. Biochem., 56, 779, 1987, P. J. Casey et al., Natl. Acad. Sci. U.S.A. 86, 8323, 1989).

The transformed ras proteins, e.g., H-Ras, N-Ras, K-RasA, K-RasB etc., translated by the mutated ras gene, in activated state, result in the unregulated cell growth, thereby causing cell tumorization. Especially, the mutated ras genes are found in patients suffered from

various cancers, e.g., colon cancer (about 50%), pancreas cancer (about 90%), lung cancer (about 50%), and thyroid gland cancer (about 30%) (S. Rodenhuis, Semin. Cancer Biol. 3, 241, 1992).

Various researches have been carried out to develop ras inhibitors. Most of the researches have been focused on FPTase inhibitors, which may inhibit the translocation of ras proteins into an intracellular membrane. For example, Cys-Val-Phe-Met mimetic derivatives, mimic to C-terminal of ras protein(Cys-A1-A2-Met), are disclosed (J. L. Goldstein et al., J. Biol. Chem., 266, 15575, 1991; A. M. Garcia et al., J. Biol. Chem., 268, 18415, 1993; S. L. Graham et al., J. Med. Chem., 37, 725, 1994).

Various derivatives mimicking Cys-Ile-Phe-Met as a prototype inhibitor, such as for example, alkylamine derivatives wherein Phe-Met moiety is displaced by aromatic alkylamine (S. J. Desolms et al., J. Med. Chem., 38, 3967, 1995) and carbonylamide derivatives wherein aminomethylnaphthalene is combined with cysteine and trans-3(S)-ethylproline(WO9606609, 1996), were disclosed to have FPTase inhibitory activity. And pseudopeptide derivatives containing substituted imidazolethyl group instead of cysteine were disclosed to have FPTase inhibitory activity (J. H. Hunt et al., J. Med. chem., 39, 353, 1996; WO9610035, 1996; WO9610034, 1996; WO9609836, 1996). And also, WO9639173 disclosed that compounds containing p-cyanobenzyl-imidazolacetate instead of cysteine and N-naphthylmethyl instead of phenylalanine, respectively, in the structure of Cys-Ile-Phe-Met, have FPTase inhibitory activity.

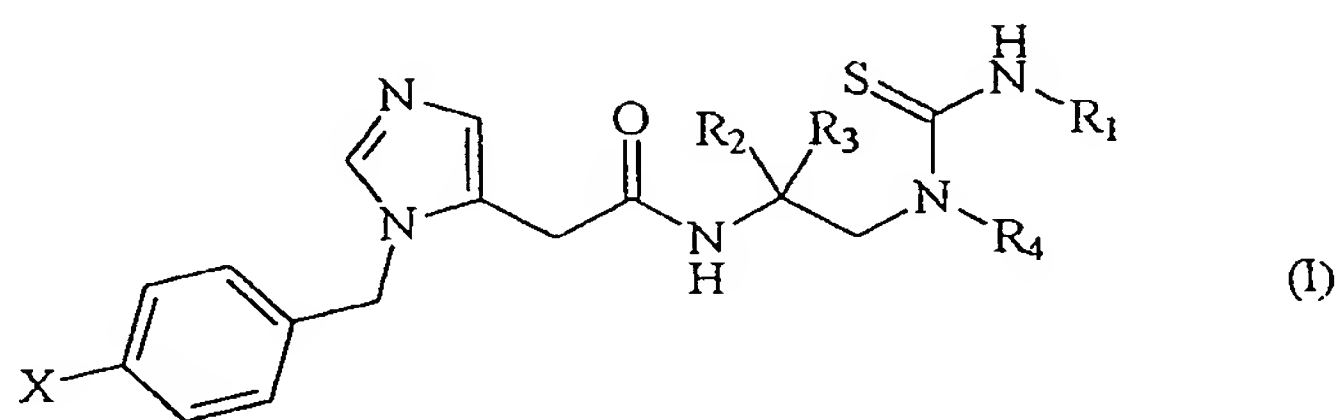
However, it has been pointed out that the FPTase inhibitors described in the above can not effectively inhibit the farnesylation of the

K-ras protein, which is the most frequently found ras-protein in human cancer. It is the reason why FPTase inhibitors fail to inhibit the prenylation of the K-ras protein in cells that the K-ras protein suppressed by FPTase inhibitors keeps its activity by using GGPTase instead of FPTase (G. L. James et al., J. Biol. Chem. 270, 6221, 1995).

DISCLOSURE OF INVENTION

Therefore, the present inventors have extensively researched to develop ras-transformed cell growth inhibitors, which can block the prenylation of the K-ras protein; and, as a result, have discovered that novel thiourea derivatives of the following formula (I) exhibit excellent activity for inhibiting K-ras prenylation as well as ras-transformed cell (per se) growth.

Accordingly, it is a primary object of the present invention to provide thiourea derivatives represented by the following formula (I):



pharmaceutically acceptable salt or stereoisomer thereof, wherein

R₁ represents hydrogen; straight-chain or branched C₁-C₈-alkyl which is optionally substituted by substituents selected from a group consisting of halogen, C₁-C₆-alkoxy, C₁-C₆-alkoxycarbonyl and

di(C₁-C₄-alkyl)amino; C₂-C₆-alkenyl; C₁-C₄-alkoxycarbonyl; C₃-C₆-cycloalkyl; phenyl which is optionally mono- to trisubstituted by substituents selected from a group consisting of halogen, C₁-C₆-alkyl, C₁-C₆-alkoxy, C₁-C₆-alkylthio, halogeno-C₁-C₆-alkyl, azido, nitro, amino, phenyl, di(C₁-C₄-alkyl)amino and hydroxy; phenyl-C₁-C₄-alkyl; naphthyl which is optionally substituted by di(C₁-C₄-alkyl)amino; benzoyl; pyridyl which is optionally substituted by substituents selected from a group consisting of halogen and C₁-C₆-alkoxy; or adamantyl,

R₂ and R₃ independently of one another represent hydrogen, straight-chain or branched C₁-C₆-alkyl, C₃-C₆-cycloalkyl or benzyloxybenzyl,

R₄ represents C₁-C₄-alkyl substituted by phenyl wherein the phenyl moiety is optionally mono- to trisubstituted by substituents selected from a group consisting of halogen, halogeno-C₁-C₄-alkyl, C₁-C₄-alkylenedioxy, C₁-C₆-alkyl, nitro, C₁-C₆-alkoxy, carboxyl and C₁-C₆-alkoxycarbonyl; naphthyl-C₁-C₄-alkyl; thiophenyl-C₁-C₄-alkyl; C₁-C₆-alkyl which is optionally substituted by substituents selected from a group consisting of pyridyl, oxypyridyl, C₁-C₆-alkoxy and C₁-C₆-alkylthio; or C₂-C₆-alkynyl, and

X represents nitro or cyano.

It is another object of the present invention to provide processes for preparing the compound of formula (I).

It is a further object of the present invention to provide a

pharmaceutical composition comprising the compound of formula (I) as an active ingredient together with a pharmaceutically acceptable carrier.

BEST MODE FOR CARRYING OUT THE INVENTION

The thiourea derivatives of the present invention may be pharmaceutically acceptable non-toxic salt forms. The non-toxic salts may include conventional acid addition salts used in the field of anticancer agents, e.g., salts originated from inorganic acid such as hydrochloric acid, hydrobromic acid, sulfonic acid, sulfamic acid, phosphoric acid, or nitric acid, and organic acid such as acetic acid, propionic acid, succinic acid, glycolic acid, stearic acid, malic acid, hydroxymalic acid, phenylacetic acid, glutamic acid, benzoic acid, salicylic acid, sulfanyl acid, 2-acetoxybenzoic acid, fumaric acid, toluenesulfonic acid, methandisulfonic acid, ethandisulfonic acid, oxalic acid, trifluoroacetic acid. Such acid addition salts may be prepared in accordance with any of the conventional methods.

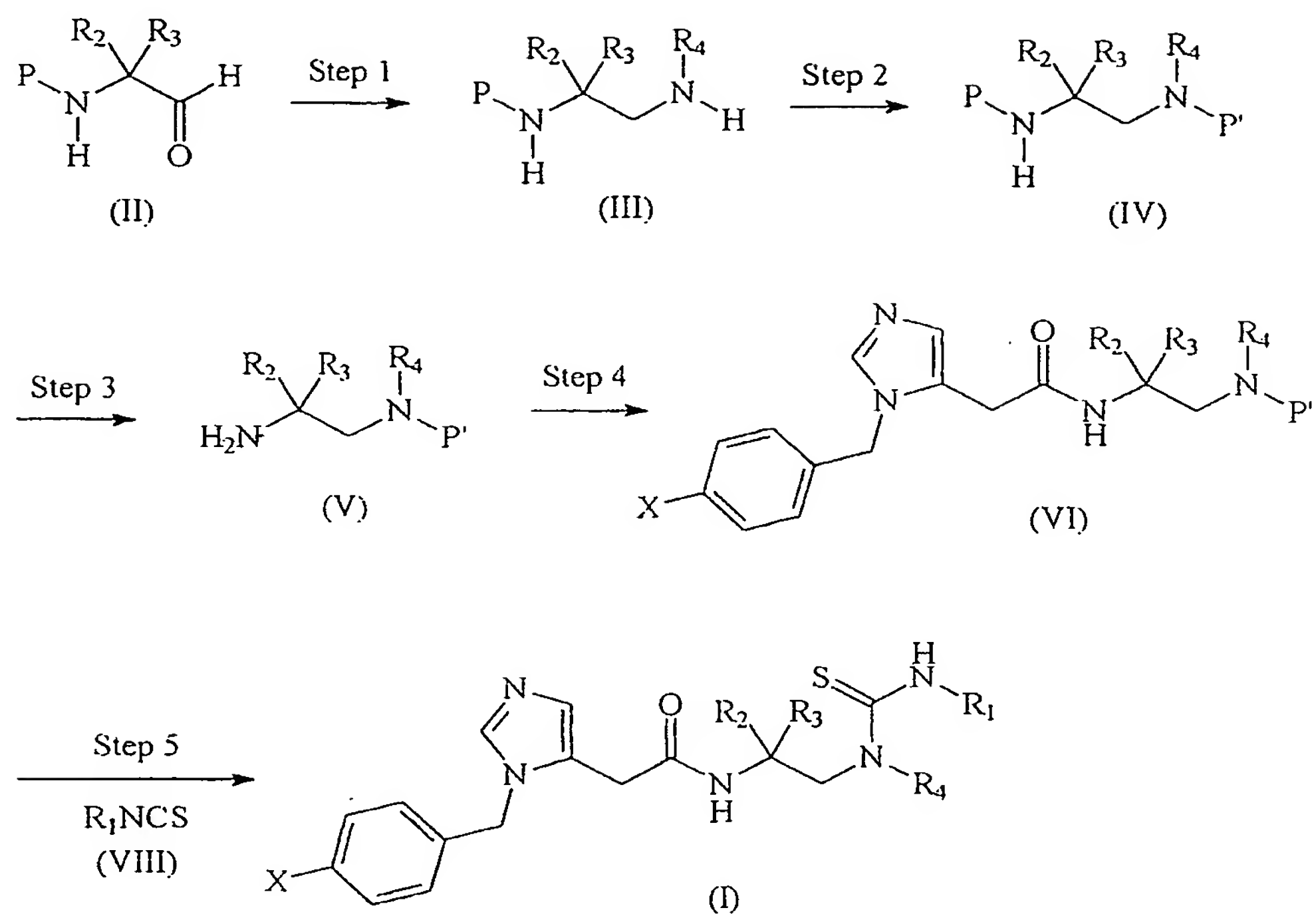
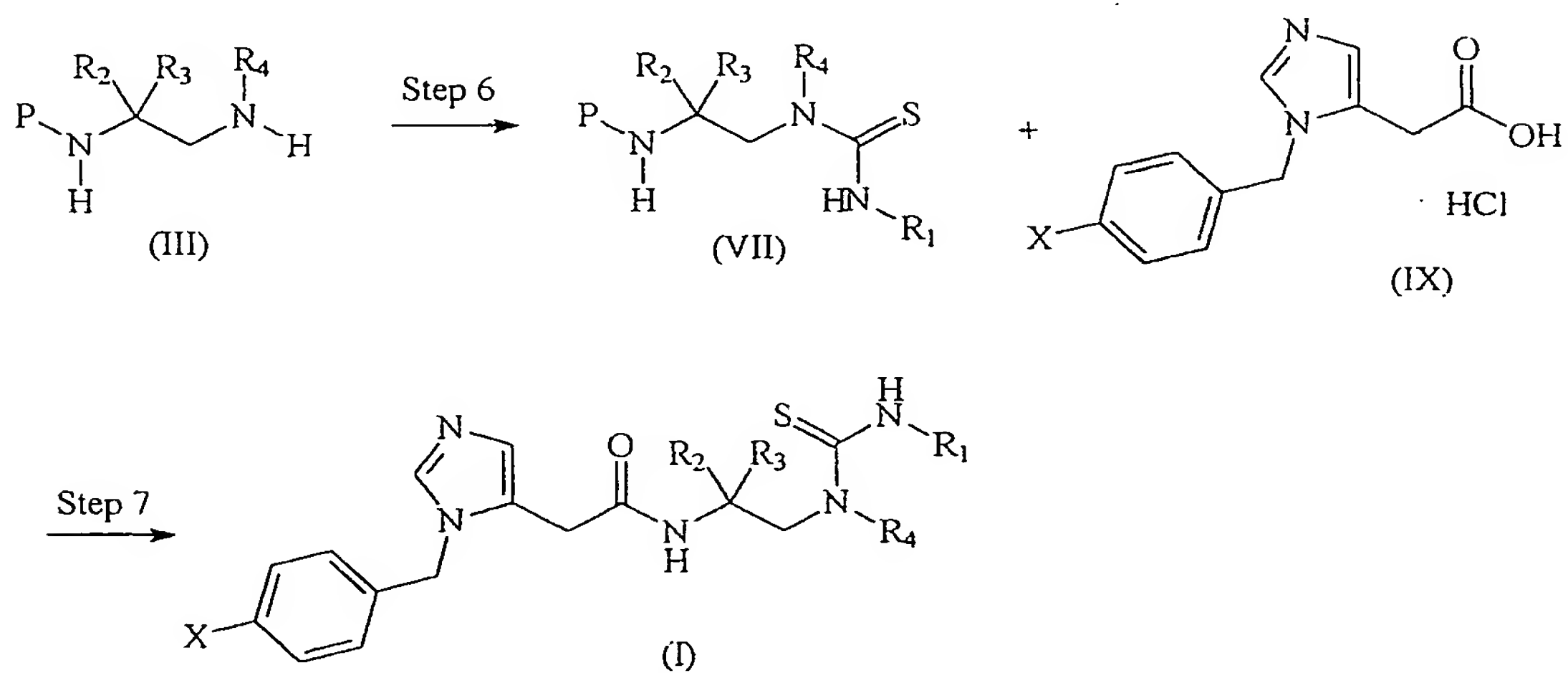
Since the compound of formula (I) according to the present invention may have asymmetric carbon atoms depending on the substituents, they can be present in the form of racemate, diastereomer mixture or the individual stereospecific isomers. Thus, the present invention also includes all of these stereoisomers and their mixtures.

Among the compound of formula (I) according to the present invention, the preferred compounds include those wherein

R₁ represents phenyl which is optionally mono- to trisubstituted by substituents selected from a group consisting of halogen, C₁-C₆-alkyl, C₁-C₆-alkoxy, C₁-C₆-alkylthio, halogeno-C₁-C₆-alkyl, azido, nitro, amino, phenyl, di(C₁-C₄-alkyl)amino and hydroxy; or

pyridyl which is optionally substituted by substituents selected from a group consisting of halogen and C₁-C₆-alkoxy, R₂ and R₃ independently of one another represent straight-chain or branched C₁-C₆-alkyl, R₄ represents C₁-C₄-alkyl substituted by phenyl wherein the phenyl moiety is optionally mono- to trisubstituted by substituents selected from a group consisting of halogen, halogeno-C₁-C₄-alkyl, C₁-C₄-alkylenedioxy, C₁-C₆-alkyl, nitro, C₁-C₆-alkoxy, carboxyl and C₁-C₆-alkoxycarbonyl; and X represents nitro or cyano.

The present invention includes, within its scope, processes for the preparation of a thiourea derivative of formula (I) or non-toxic salts thereof. The compound of formula (I) may be prepared in accordance with Scheme 1 or Scheme 2 described below :

Reaction Scheme 1Reaction Scheme 2

In the above Scheme 1 and 2,
R₁, R₂, R₃, R₄ and X are defined as previously described, and
P and P' independently of one another represent amino-protecting group.

In the present invention, the amino-protecting group may be selected from conventional ones, such as for example, fluorenylmethyloxycarbonyl(Fmoc), t-butoxycarbonyl(Boc) and benzyloxycarbonyl(Cbz).

The processes summarized in the above Reaction Scheme 1 and 2 will be more specifically explained in the following.

Step 1. Reductive Alkylation

The aldehyde derivative protected with an amino-protecting group such as t-butoxycarbonyl may be synthesized in accordance with conventional methods (Org. Syn. Vol. 67, 1988, 69 and Synthesis, 1983, 676). That is, the aldehyde derivative may be reacted with R₄-amine in the presence of sodium cyanoborohydride or other conventional reducing agent to give the compound of formula (III). This reaction can be facilitated by the addition of potassium acetate or acetic acid and 3A molecular seive.

Step 2. Amino Protection

The compound of formula (III) may be protected by a conventional amino-protecting group, e.g. 9-fluorenylmethyloxycarbonyl, to give a compound of formula (IV).

Step 3. Deprotectoin

The compound of formula (IV) having two kinds of amino-protecting group may be dissolved in an appropriate organic solvent and then reacted with deprotecting agent, e.g., trifluoroacetic acid, to remove selectively one of the two amino-protecting groups.

Step 4. Amide Bond Formation

The compound of formula (V) may be reacted with 1-substituted-1H-imidazol-5-ylacetic acid hydrochloride in a solvent in the presence of an appropriate coupling agent to give a compound of formula (VI). The coupling agent may be one or more selected from conventional catalysts, e.g., hydroxybenzotriazole, dialkylcarbodiimide and triethylamine. The preferable solvent may be dimethylformamide, methylene chloride, or a mixture thereof.

Step 5. Deprotection and Addition

The compound of formula (VI) having an amino-protecting group may be dissolved in an appropriate organic solvent, e.g., dimethylformamide or methylene chloride, and then reacted with deprotecting agent, e.g., piperidine, to remove the amino-protecting group. Then, the resulting deprotected compound may be reacted with a substituted isothiocyanate of formula (VIII) in a solvent such as methylene chloride to give the desired compound of formula (I).

Step 6. Addition

The compound of formula (III) having an amino group may be reacted with substituted isothiocyanate in an appropriate solvent to give a compound of formula (VII). The solvent may be selected from

dimethylformamide, methylene chloride and acetonitrile.

Step 7. Deprotection and Amide Bond Formation

The compound of formula (VII) having an amino-protecting group may be dissolved in an organic solvent, such as dimethylformamide, methylene chloride, etc., and reacted with deprotecting agent, such as piperidine, to remove the protecting group. The resulting compound is then reacted with 1-substituted-1H-imidazol-5-ylacetic acid hydrochloride of formula (IX) in the presence of an appropriate coupling agent to give the compound of formula (I). The coupling agent may be one or more selected from conventional catalysts, e.g. hydroxybenzotriazole, dialkylcarbodiimide and triethylamine. And as the solvent, dimethylformamide, methylene chloride, or a mixture thereof can be mentioned.

The non-toxic pharmaceutically acceptable salts of the compound (I) may be prepared according to the conventional methods known per se in the art from the compound (I). Generally, they are prepared by reacting the organic bases in an appropriate solvent or solvent mixture with a salt-forming inorganic or organic acid in a stoichiometric amount or in excess.

The present invention also includes within its scope a pharmaceutical composition for inhibition of ras-transformed cell growth comprising a therapeutically effective amount of the novel compound of formula (I), as defined above, or a pharmaceutically acceptable salt thereof as an active ingredient together with a pharmaceutically acceptable carrier.

The composition of the present invention may include additives such as lactose or corn starch, lubricant such as magnesium stearate, or conventional emulsifier, suspending agent, stabilizer, isotonic agent. If necessary, sweetner and/or flavoring agent may be added.

The composition of the present invention may be administered orally or parenterally, including intravenous, intraperitoneal, subcutaneous, rectal and topical routes of administration. Therefore, the composition of the present invention may be formulated into various forms such as tablets, capsules, aqueous solutions or suspensions. In case of tablets for oral use, carriers such as lactose, corn starch, and lubricating agents, e.g. magnesium stearate, are commonly added. For oral administration in capsule form, lactose and/or dried corn starch can be used as a diluent. When an aqueous suspension are required for oral use, the active ingredient may be combined with emulsifying and/or suspending agents. If desired, certain sweeteners and/or flavoring agents may be added. For intramuscular, intraperitoneal, subcutaneous and intravenous use, sterile solutions of the active ingredient are usually prepared, and the pH of the solutions should be suitably adjusted and buffered. For intravenous use, the total concentration of solutes should be controlled in order to render the preparation isotonic. The composition of the present invention may be in the form of aqueous solution containing pharmaceutically acceptable carriers, e.g., saline, at a pH level of 7.4. The solutions may be introduced into a patient's intramuscular blood-stream by local bolus injection.

The compounds of the present invention may be administered in an effective amount ranging from about 0.1mg/kg to about 20mg/kg, preferably from about 0.5mg/kg to about 10mg/kg, per day into a subject patient suffered from various cancers, e.g., colorectal carcinoma, exocrine

pancreatic carcinoma, and myeloid leukemias. Of course, the dosage may be changed according to patient's age, weight, susceptibility, or symptom.

The following Examples are given for the purpose of illustration only, and are not intended to limit the scope of the invention.

Preparative Example 1

1-(4-Nitrobenzyl)-1H-imidazol-5-ylacetic acid HCl

<Step 1>

1H-Imidazol-4-ylacetic acid methyl ester HCl

Hydrogen chloride gas was bubbled through a solution of 1H-imidazol-4-ylacetic acid hydrochloride (10.0 g, 61.5 mmol) in methanol (200 ml) until saturated. The solution was allowed to stand for 18h at room temperature and then concentrated *in vacuo* to give the title compound (11.6 g, 100%) as a white solid.

¹H-NMR (DMSO-d₆) : δ 9.05(s, 1H), 7.50(s, 1H), 3.90(s, 2H), 3.60(s, 3H).

<Step 2>

1-(Triphenylmethyl)-1H-imidazol-4-ylacetic acid methyl ester

To a suspension of 1H-imidazol-4-ylacetic acid methyl ester HCl (11.6 g, 65.6 mmol) in dichloromethane (350 ml) and DMF (50 ml) were added triethylamine (27.4 ml, 196.6 mmol) and triphenylmethyl chloride (21.9 g, 78.6 mmol). The mixture was stirred for 15hr. The reaction mixture was washed with water and brine. The organic layer was concentrated *in vacuo* and purified by silica gel column chromatography(eluent: EtOAc/n-hexane=2/1, v/v) to provide a white solid of the title compound (7.44 g, 74 % in 2 steps).

TLC : $R_f = 0.20$ (EtOAc / n-hexane = 1 / 1)

$^1\text{H-NMR}$ (CDCl_3) : δ 7.45(s, 1H), 7.05-7.45(m, 15H), 6.75(s, 1H), 3.70(s, 2H)

<Step 3>

1-(4-Nitrobenzyl)-1H-imidazol-5-ylacetic acid methyl ester

To a solution of 1-triphenylmethyl-1H-imidazol-4-ylacetic acid methyl ester (4.96 g, 13.0 mmol) in acetonitrile (100 ml) was added 4-nitrobenzylbromide (2.80 g, 13.0 mmol) and the mixture was heated to 65°C for 24hr. The reaction mixture was concentrated to dryness, dissolved in methanol (150 ml) and heated to reflux temperature for 1hr. The solution was concentrated *in vacuo* to the volume of 50 ml. Crystallization from methanol gave the title compound (3.27 g, 92 %) as a white solid.

TLC : $R_f = 0.50$ (CH_2Cl_2 / MeOH = 9 / 1)

$^1\text{H-NMR}$ (DMSO-d_6) : δ 9.35(s, 1H), 8.25(d, 2H), 7.70(s, 1H), 7.60(d, 2H), 5.70(s, 2H), 3.95(s, 2H), 3.50(s, 3H)

<Step 4>

1-(4-Nitrobenzyl)-1H-imidazol-5-ylacetic acid HCl

A solution of 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid methyl ester (3.30 g, 11.9 mmol) in 1N HCl (25 ml) was heated at 60°C for 4hr and concentrated *in vacuo* to dryness. Crystallization from methanol gave the title compound (1.64 g, 53 %) as a white solid.

$^1\text{H-NMR}$ (DMSO-d_6) : δ 9.45(s, 1H), 8.30(d, 2H), 7.70(s, 1H), 7.60(d, 2H), 5.70(s, 2H), 3.80(s, 2H)

Preparative Example 2.

1-(4-Cyanobenzyl)-1H-imidazol-5-ylacetic acid HCl

<Step 1>

1-(4-Cyanobenzyl)-1H-imidazol-5-ylacetic acid methyl ester

The title compound (0.89 g, 93 %) was prepared from 1-(triphenylmethyl)-1H-imidazol-4-ylacetic acid methyl ester (1.43 g, 3.74 mmol) and 4-cyanobenzylbromide (0.81 g, 4.11 mmol) according to the same reaction as described in <Step 3> of Preparative Example 1.

¹H-NMR (DMSO-d₆) : δ 9.30(s, 1H), 7.95(d, 2H), 7.70(s, 1H), 7.52(d, 2H), 5.65(s, 2H), 3.92(s, 2H), 3.50(s, 3H)

<Step 2>

1-(4-Cyanobenzyl)-1H-imidazol-5-ylacetic acid HCl

The title compound (0.76 g, 90 %) as a white solid was prepared from 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid methyl ester (0.86 g, 3.37 mmol) and 1.0 N HCl (50 ml) according to the same reaction as described in <Step 4> of Preparative Example 1.

¹H-NMR (DMSO-d₆) : δ 14.60(bs, 1H), 12.95(bs, 1H), 9.35(s, 1H), 7.95(d, 2H), 7.65(s, 1H), 5.60(s, 2H), 3.80(s, 2H)

Preparative Example 3

N-t-Butoxycarbonyl-L-isoleucine aldehyde

<Step 1>

N-t-Butoxycarbonyl-L-isoleucine-N'-methoxy-N'-methanamide

To a suspension of N,O-dimethylhydroxylamine HCl (6.1 g, 62.5 mmol) in methylene chloride (60 ml) was added N-methyl morpholine (7.6 ml, 69.1 mmol) dropwise at -10°C, and this solution was stored at

the same temperature. A solution of N-t-butoxycarbonyl-L-isoleucine (15 g, 62.4 mmol), N-methylmorpholine (7.6 ml, 69.1 mmol) and isobutylchloroformate (8.1 ml, 62.4 mmol) in methylene chloride (300 ml) was added dropwise to the solution of N,O-dimethylhydroxylamine prepared above, and stirred overnight at room temperature. After the addition of water (100 ml), the mixture was extracted with ethylacetate (100 ml X 3). The organic phase was washed with water (100 ml x 2) and brine (100 ml), dried over MgSO_4 , and concentrated *in vacuo*. The residue was purified by silica gel column chromatography(eluent: ethylacetate/n-hexane=1/4, v/v), to give an oil of the title compound (15.1 g, 89%).

TLC : $R_f = 0.25$ (EtOAc /n-hexane / EtOH = 25 / 100 / 2)

$^1\text{H-NMR}$ (CDCl_3) : δ 5.20(d, 1H), 4.60(m, 1H), 3.70(d, 3H), 3.20(d, 3H), 2.00(m, 1H), 1.40(s, 9H), 1.00(m, 8H)

<Step 2>

N-t-Butoxycarbonyl-L-isoleucine aldehyde

To a suspension of LiAlH_4 (2.4 g, 54.7 mmol) in dry THF (300 ml) was added dropwise a solution of N-t-butoxycarbonyl-L-isoleucine -N'-methoxy-N'-methanamide (15 g, 54.7 mmol) in dry THF (30 ml) while maintaining a temperature at -45°C or less. After the addition, the aqueous potassium bisulfate solution (12.7 g / 35 mL) was added dropwise while maintaining a temperature of -35°C , and then the reaction mixture was warmed to room temperature. The reaction mixture was mixed with an adequate amount of celite, and stirred for 1 hr. After the removal of celite by filtration, the organic phase was washed with water, dried over MgSO_4 , and concentrated *in vacuo* to give an oil of the title compound (8.2 g, 69%).

TLC : $R_f = 0.55$ (EtOAc / n-hexane / EtOH = 25 / 100 / 2)

$^1\text{H-NMR}$ (CDCl_3) : δ 9.70(s, 1H), 5.20(d, 1H), 4.30(m, 1H), 2.00(m, 1H), 1.50(s, 9H), 1.00(m, 8H)

Preparative Example 4

N-(2,3-Dichlorobenzyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

<Step 1>

N-(2,3-Dichlorobenzyl)-2(S)-(t-butoxycarbonyl)amino-3(S)-methylpentylamine

To a solution of N-t-butoxycarbonyl-L-isoleucine aldehyde (4.52 g, 21.0 mmol) prepared from Preparative Example 3 in methanol (50 ml) were added 2,3-dichlorobenzylamine (4.07 g, 23.1 mmol), acetic acid (0.5 ml), and molecular sieve (3A, 5 g), and followed by sodium cyanoborohydride (1.45 g, 21.0 mmol). The mixture was stirred for overnight at room temperature. After the removal of insoluble material by filtration, the filtrate was concentrated *in vacuo*. The residue was poured into water (100 ml), extracted with ethylacetate (100 ml). The organic layer was dried over MgSO_4 , and concentrated *in vacuo*. The residue was purified by silica gel column chromatography(eluent: ethylacetate/n-hexane=1/3, v/v), to give a light yellow oil of the title compound (5.0 g, 63%).

TLC : $R_f = 0.49$ (CH_2Cl_2 / MeOH = 10 / 1)

$^1\text{H-NMR}$ (CDCl_3) : δ 7.08-7.40(m, 3H), 4.70(d, 1H), 3.83(m, 2H), 3.60(m, 1H), 2.45-2.75(m, 2H), 1.30-1.60(m, 11H), 0.97-1.20(m, 1H), 0.75-0.95(m, 6H)

<Step 2>

N-(2,3-Dichlorobenzyl)-N-(9-fluorenylmethyloxycarbonyl)-2(S)-(t-butoxycarbonyl)amino-3(S)-methylpentylamine

To a solution of N-(2,3-dichlorobenzyl)-2(S)-(t-butoxycarbonyl)amino-3(S)-methylpentylamine (2.79 g, 7.39 mmol) in dichloromethane (30 ml) was added triethylamine (1.54 ml, 11.08 mmol) dropwise. After cooling to 0°C, the solution of 9-fluorenylmethylchloroformate (2.29 g, 8.87 mmol) in dichloromethane (20 ml) was added, and the mixture was stirred for overnight at room temperature. The reaction mixture was diluted with dichloromethane (100 ml), and washed with 5% HCl, saturated sodium bicarbonate solution, and brine several times. The organic phase was dried over MgSO₄, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography(eluent: ethylacetate/n-hexane=1/5, v/v), to give a white solid of the title compound (2.42 g, 55%).

TLC : R_f = 0.29 (EtOAc / n-hexane = 1 / 4)

¹H-NMR (CDCl₃) : δ 7.52-7.83(m, 3H), 7.23-7.52(m, 5H), 7.00-7.22(m, 2H), 6.85(d, 1H), 4.62-4.95(m, 2H), 4.28-4.62(m, 3H), 4.02-4.28(m, 1H), 3.40-4.00(m, 2H), 2.45-2.90(m, 1H), 1.42(d, 9H), 0.97-1.41(m, 3H), 0.70-0.95(m, 6H)

<Step 3>

N-(2,3-Dichlorobenzyl)-N-(9-fluorenylmethyloxycarbonyl)-2(S)-amino-3(S)-methylpentylamine trifluoroacetic acid salt

To a solution of N-(2,3-dichlorobenzyl)-N-(9-fluorenylmethyloxycarbonyl)-2(S)-(t-butoxycarbonyl)amino-3(S)-methylpentylamine (2.42 g) in

methylene chloride (30 ml) was added trifluoroacetic acid (10 ml) dropwise, and the mixture was stirred for 2 hr at room temperature. The reaction mixture was concentrated *in vacuo* to give an oil of the title compound, which was used for next steps without further purification.

<Step 4>

N-(2,3-Dichlorobenzyl)-N-(9-fluorenylmethyloxycarbonyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid HCl (1.05 g, 3.54 mmol) prepared from Preparative Example 1 in methylene chloride (50 ml) were added 1-hydroxybenzotriazole (0.82 g, 5.31 mmol), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (1.0 g, 4.60 mmol), and triethylamine (1.69 ml, 10.6 mmol) while stirring. After stirring for 1hr, N-(2,3-dichlorobenzyl)-N-(9-fluorenylmethyloxycarbonyl)-2(S)-amino-3(S)-methylpentylamine trifluoroacetic acid salt (2.46 g, 4.03 mmol) was added to the reaction mixture and stirred for overnight at room temperature. The reaction mixture was poured into water, the organic phase was separated, dried over MgSO₄, and concentrated *in vacuo* to give the title compound.

<Step 5>

N-(2,3-Dichlorobenzyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

N-(2,3-Dichlorobenzyl)-N-(9-fluorenylmethyloxycarbonyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine(prepared in step 4) was dissolved in dimethylformamide (14 ml), and then piperidine (6 ml) was added. The reaction mixture was stirred for 4 hr at room temperature, and then the solvent was distilled off *in vacuo*.

The residue was purified by silica gel column chromatography (eluent: methylene chloride/methanol=9/1, v/v), to give a white solid of the title compound (430 mg).

TLC : $R_f = 0.20$ (CH_2Cl_2 / MeOH = 10 / 1)

$^1\text{H-NMR}$ (CDCl_3) : δ 8.20(d, 2H), 7.58(s, 1H), 7.40(m, 1H), 7.12-7.36(m, 4H), 7.05(s, 1H), 5.70-6.00(m, 1H), 5.33(s, 2H), 3.75-4.10(m, 3H), 3.38(s, 2H), 2.62(d, 2H), 1.78(bs, 1H), 1.42-1.65(m, 1H), 1.22-1.42(m, 1H), 0.96-1.22(m, 1H), 0.75-0.95(m, 6H)

Preparative Example 5

N-(2,3-Dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

1-(4-Cyanobenzyl)-1H-imidazol-5-ylacetic acid HCl was reacted according to the same procedure as Steps 4 and 5 of Preparative Example 4 to give the title compound.

TLC : $R_f = 0.35$ (CH_2Cl_2 / MeOH = 10 / 1)

$^1\text{H-NMR}$ (CDCl_3) : δ 7.62(d, 2H), 7.53(s, 1H), 7.40(m, 3H), 7.00-7.35(m, 5H), 5.92(d, 1H), 5.22(s, 2H), 3.75-4.05(m, 3H), 3.38(s, 2H), 2.62(m, 2H), 1.82(bs, 1H), 1.42-1.65(m, 2H), 1.22-1.42(m, 1H), 0.96-1.22(m, 1H), 0.75-0.95(m, 6H)

Preparative Example 6

N-(1-Naphthylmethyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

<Step 1>

N-(1-Naphthylmethyl)-2(S)-(*t*-butoxycarbonyl)amino-3(S)-methylpentylamine

A solution of 1-naphthylmethylamine (0.90 g, 5.71 mmol) in methanol (10 ml) was adjusted to pH 6 by the addition of triethylamine. Then, sodium cyanoborohydride (8.60 ml, 1M solution in tetrahydrofuran), potassium acetate (562 mg, 5.71 mmol), and molecular sieves (2.00 g) were added thereto at 0°C under nitrogen. N-*t*-Butoxycarbonyl-L-isoleucine aldehyde (1.23 g, 5.71 mmol) in methanol was added dropwise to above solution. The reaction mixture was stirred at 20°C under nitrogen for 2hr. After concentration *in vacuo*, the residue was partitioned between water and ethyl acetate. The organic layer was washed with saturated sodium bicarbonate solution and brine, dried over MgSO₄ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography(eluent: EtOAc /n-hexane=1/3, v/v) to give the title compound (740 mg, 36 %) as a white solid.

TLC : R_f = 0.20 (EtOAc / n-hexane = 1 / 2)

¹H-NMR (CDCl₃) : δ 7.40-8.25(m, 7H), 4.65(d, 1H), 4.15-4.40(m, 2H), 3.60-3.80(m, 1H), 2.70-2.90(m, 2H), 1.40-1.70(m, 13H), 0.80-1.00(m, 6H)

<Step 2>

N-(1-Naphthylmethyl)-N-(9-fluorenylmethyloxycarbonyl)-2(S)-(t-butoxycarbonyl)amino-3(S)-methylpentylamine

To a solution of N-(1-naphthylmethyl)-2(S)-(t-butoxycarbonyl)amino-3(S)-methylpentylamine (1.00 g, 2.81 mmol) in dichloromethane (10 ml) was added triethylamine (0.47 ml, 3.37 mmol) dropwise. The reaction mixture was cooled to 0°C. A solution of 9-fluorenylmethylchloroformate (798 mg, 3.09 mmol) in dichloromethane (5 ml) was added dropwise thereto. The reaction mixture was stirred at room temperature for 2hr. After concentration *in vacuo*, the residue was partitioned between 5%

HCl and ethyl acetate. The organic layer was washed with saturated sodium bicarbonate solution and brine, dried over MgSO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography(eluent: EtOAc/n-hexane=1/5, v/v) to give the title compound (1.39 g, 86 %) as a white solid.

TLC : $R_f = 0.36$ (EtOAc / n-hexane = 1 / 5)

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 15H), 5.33(m, 1H), 4.62-5.05(m, 2H), 4.40-4.60(m, 1H), 4.10-4.38(m, 1H), 3.80-4.08(m, 2H), 2.40-3.00(m, 2H), 1.43(d, 9H), 0.95-1.40(m, 3H), 0.50-0.95(m, 6H)

<Step 3>

N-(1-Naphthylmethyl)-N-(9-fluorenylmethyloxycarbonyl)-2(S)-amino-3(S)-methylpentylamine trifluoroacetic acid salt

N-(1-Naphthylmethyl)-N-(9-fluorenylmethyloxycarbonyl)-2(S)-(*t*-butoxycarbonyl)amino-3(S)-methylpentylamine (827 mg, 1.43 mmol) was dissolved in dichloromethane (30 ml) and trifluoroacetic acid (10 ml) was added thereto. The reaction mixture was stirred for 2hr at room temperature and then concentrated to dryness to give the title compound.

<Step 4>

N-(1-Naphthylmethyl)-N-(9-fluorenylmethyloxycarbonyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid HCl (140 mg, 0.54 mmol) from Preparative Example 1 in dry dichloromethane / dry dimethylformamide (10 ml / 3 ml) were added 1-hydroxybenzotriazole(HOBt) (109 mg, 0.80 mmol), 1-ethyl-3-(3-dimethyl-aminopropyl)carbodiimide(EDC) (154 mg, 0.80 mmol) and triethylamine

(0.19 ml, 1.34 mmol). The reaction mixture was stirred for 30 min. N-(1-naphthylmethyl)-N-(9-fluorenylmethyloxycarbonyl)-2(S)-amino-3(S)-methylpentylamine trifluoroacetic acid salt (318 mg, 0.54 mmol) was added to this solution. After concentration *in vacuo*, the residue was partitioned between water and ethyl acetate. The organic layer was washed with saturated sodium bicarbonate solution and brine, dried over MgSO_4 and concentrated *in vacuo*. The residue was purified by silica gel column chromatography(eluent: $\text{CH}_2\text{Cl}_2/\text{MeOH}=10/1$, v/v) to give the title compound (249 mg, 63 %) as a white solid.

TLC : $R_f = 0.50$ ($\text{CH}_2\text{Cl}_2 / \text{MeOH} = 10 / 1$)

$^1\text{H-NMR}$ (CDCl_3) : δ 6.90-8.25(m, 21H), 6.28(d, 1H), 5.31(s, 2H), 5.20(dd, 2H), 4.02(bs, 1H), 4.08-4.97(m, 3H), 3.78(t, 1H), 2.93(d, 2H), 1.48(m, 1H), 1.26(m, 1H), 0.68-1.16(m, 7H)

<Step 5>

N-(1-Naphthylmethyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

N-(1-Naphthylmethyl)-N-(9-fluorenylmethyloxycarbonyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine(249 mg, 0.34 mmol) was dissolved in dimethylformamide (8 ml) and piperidine (2 ml). The reaction solution was stirred at room temperature for 2hr. The solvents were removed by distillation *in vacuo*. The residue was purified by silica gel column chromatography(eluent: $\text{CH}_2\text{Cl}_2/\text{MeOH}=10/1$, v/v) to give the title compound (116 mg, 68 %) as a white solid.

TLC : $R_f = 0.40$ ($\text{CH}_2\text{Cl}_2 / \text{MeOH} = 10 / 1$)

$^1\text{H-NMR}$ (CDCl_3) : δ 6.90-8.20(m, 13H), 5.80(d, 1H), 5.04(dd, 2H), 4.22(s, 2H), 3.90(bs, 1H), 3.18(dd, 2H), 2.78(d, 2H), 1.48(m, 1H),

1.26(m, 1H), 1.04(m, 1H), 0.87(m, 6H)

Example 1

N-(2,3-Dichlorobenzyl)-N-(benzylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of N-(2,3-dichlorobenzyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}-amino-3(S)-methylpentylamine in methylenechloride (0.02M, 1ml; 0.02mmol) was added benzylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 5hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: methylene chloride/methanol=9/1, v/v) to give the title compounds as a white solid.

¹H-NMR (CDCl₃) : δ 6.90-8.20(m, 14H), 6.02(bs, 1H), 5.32(s, 2H), 5.15(m, 1H), 4.80(d, 2H), 4.60(m, 2H), 4.15(m, 1H), 3.25(s, 2H), 3.04(dd, 1H), 1.60(m, 1H), 1.42(m, 1H), 1.05(m, 1H), 0.92(d, 6H)

Examples 2-26.

N-(2,3-Dichlorobenzyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine was reacted with the corresponding isothiocyanates under the same condition as described in Example 1 to give the title compounds.

Example 2

N-(2,3-Dichlorobenzyl)-N-(2-bromophenyl)thiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.02-8.18(m, 13H), 5.32(s, 2H), 5.10(m, 2H),

4.78(dd, 1H), 4.35(m, 1H), 3.40(s, 2H), 3.10(dd, 1H), 1.60(m, 1H), 1.40(m, 1H), 1.05(m, 1H), 0.92(m, 6H)

Example 3

N-(2,3-Dichlorobenzyl)-N-(3-bromophenyl)thiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-8.20(m, 13H), 5.35(s, 2H), 4.82(m, 2H), 4.65(dd, 1H), 4.18(m, 1H), 3.35(s, 2H), 3.10(dd, 1H), 1.65(m, 1H), 1.42(m, 1H), 1.05(m, 1H), 0.92(m, 6H)

Example 4

N-(2,3-Dichlorobenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-8.20(m, 13H), 5.32(s, 2H), 4.90-5.22(m, 2H), 4.65(dd, 1H), 4.20(m, 1H), 3.37(s, 2H), 3.10(dd, 1H), 1.65(m, 1H), 1.42(m, 1H), 1.05(m, 1H), 0.90(m, 6H)

Example 5

N-(2,3-Dichlorobenzyl)-N-(ethylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.90-8.22(m, 9H), 5.40(d, 2H), 4.75-5.10(m, 2H), 4.55(dd, 1H), 4.10(m, 1H), 3.62(m, 2H), 3.38(s, 2H), 3.00(dd, 1H), 1.65(m, 1H), 1.45(m, 1H), 1.10(m, 3H), 1.05(m, 1H), 0.92(m, 6H)

Example 6

N-(2,3-Dichlorobenzyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.02-8.20(m, 13H), 5.38(s, 2H), 5.10(m, 2H), 4.72(dd, 1H), 4.22(m, 1H), 3.38(s, 2H), 3.10(dd, 1H), 1.62(m, 1H), 1.43(m, 1H), 1.10(m, 1H), 0.90(m, 6H)

Example 7

N-(2,3-Dichlorobenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.90-8.18(m, 13H), 5.35(d, 2H), 4.90-5.20(m, 2H), 4.65(dd, 1H), 4.18(m, 1H), 3.38(s, 2H), 3.15(dd, 1H), 1.60(m, 1H), 1.42(m, 1H), 1.10(m, 1H), 0.92(m, 6H)

Example 8

N-(2,3-Dichlorobenzyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.80-8.18(m, 13H), 5.38(d, 2H), 4.95-5.20(m, 2H), 4.68(dd, 1H), 4.15(m, 1H), 3.38(s, 2H), 3.10(dd, 1H), 1.60(m, 1H), 1.42(m, 1H), 1.10(m, 1H), 0.92(t, 6H)

Example 9

N-(2,3-Dichlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.82-8.20(m, 13H), 5.35(s, 2H), 5.05(m, 2H), 4.68(dd, 1H), 4.18(m, 1H), 3.78(s, 3H), 3.35(s, 2H), 3.08(dd, 1H), 1.60(m, 1H), 1.40(m, 1H), 1.10(m, 1H), 0.90(m, 6H)

Example 10

N-(2,3-dichlorobenzyl)-N-(methylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.90-8.20(m, 9H), 5.38(s, 2H), 4.70-5.10(m, 2H), 4.50(dd, 1H), 4.10(m, 1H), 3.35(s, 2H), 3.10(d, 2H), 3.00(dd, 1H), 1.55(m, 1H), 1.40(m, 1H), 1.04(m, 1H), 0.85(m, 6H)

Example 11

N-(2,3-Dichlorobenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-8.18(m, 13H), 5.40(m, 2H), 4.85(m, 2H), 4.65(dd, 1H), 4.18(m, 1H), 3.38(s, 2H), 3.15(d, 2H), 1.60(m, 1H), 1.42(m, 1H), 1.05(m, 1H), 0.90(m, 6H)

Example 12

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-8.10(m, 12H), 5.10-5.28(m, 4H), 4.80(dd, 1H), 4.25(m, 1H), 3.35(s, 2H), 3.18(dd, 1H), 1.62(m, 1H), 1.40(m, 1H), 1.05(m, 1H), 0.90(m, 6H)

Example 13

N-(2,3-Dichlorobenzyl)-N-(1-naphthylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.85-8.18(m, 16H), 5.38(d, 2H), 5.05(bs, 1H), 4.40(d, 2H), 4.05(m, 1H), 3.28(s, 2H), 2.95(dd, 1H), 1.60(m, 1H), 1.40(m, 1H), 1.05(m, 1H), 0.88(m, 6H)

Example 14

N-(2,3-Dichlorobenzyl)-N-(phenylethylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.25(m, 14H), 5.42-5.95(m, 3H), 4.74-5.25(m, 2H), 4.60(dd, 1H), 4.20(m, 1H), 3.78(m, 1H), 3.60(m, 1H), 3.42(s, 2H), 3.07(dd, 1H), 1.60(m, 1H), 1.42(m, 1H), 1.05(m, 1H), 0.90(m, 6H)

Example 15

N-(2,3-Dichlorobenzyl)-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.05-8.20(m, 9H), 6.40(bs, 1H), 5.48(s, 2H), 4.82-5.08(m, 5H), 4.45(m, 1H), 3.55(s, 2H), 3.20(m, 1H), 1.30-1.72(5H), 1.38(m, 1H), 1.40(m, 1H), 1.05(m, 1H), 0.80-1.00(m, 9H)

Example 16

N-(2,3-Dichlorobenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.80-8.20(m, 13H), 5.35(s, 2H), 5.00(m, 2H), 4.65(dd, 1H), 4.20(m, 1H), 3.82(s, 3H), 3.32(s, 2H), 3.05(dd, 1H), 1.60(m, 1H), 1.42(m, 1H), 1.12(m, 1H), 0.92(m, 6H)

Example 17

N-(2,3-Dichlorobenzyl)-N-(benzoylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.02-8.40(m, 14H), 5.58(d, 2H), 5.05-5.42(m, 2H),

4.82(dd, 1H), 4.38(m, 1H), 3.42(s, 2H), 3.24(dd, 1H), 1.65(m, 1H), 1.45(m, 1H), 1.15(m, 1H), 1.00(m, 6H)

Example 18

N-(2,3-Dichlorobenzyl)-N-(cyclohexylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-8.40(m, 9H), 5.62(d, 2H), 4.82-5.42(m, 2H), 4.75(dd, 1H), 4.42(m, 1H), 4.30(m, 1H), 3.50(s, 2H), 3.20(dd, 1H), 1.08-2.22(m, 13H), 1.05(m, 6H)

Example 19

N-(2,3-Dichlorobenzyl)-N-[(4-dimethylamino)-1-naphthylthiocarbamoyl]-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-8.25(m, 15H), 5.25(m, 3H), 4.78-5.20(dd, 2H), 4.28(m, 1H), 3.40(s, 2H), 3.18(dd, 1H), 2.90(s, 6H), 1.65(m, 1H), 1.42(m, 1H), 1.08(m, 1H), 1.05(m, 6H)

Example 20

N-(2,3-Dichlorobenzyl)-N-(phenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.22-8.38(m, 14H), 5.22-5.58(m, 4H), 4.92(dd, 1H), 4.40(m, 1H), 3.38(s, 2H), 3.28(dd, 1H), 1.64(m, 1H), 1.40(m, 1H), 1.03(m, 1H), 1.00(m, 6H)

Example 21

N-(2,3-Dichlorobenzyl)-N-(n-propylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.10-8.22(m, 9H), 5.90(bs, 1H), 5.60(d, 2H), 4.85-5.40(m, 2H), 4.75(dd, 1H), 4.30(m, 1H), 3.64-3.85(m, 2H), 3.55(s, 2H), 3.20(dd, 1H), 1.42-1.85(m, 4H), 1.22(m, 1H), 1.05(m, 6H), 1.00(q, 3H)

Example 22

N-(2,3-Dichlorobenzyl)-N-(4-azidophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.20-8.40(m, 13H), 5.55(d, 2H), 5.04-5.45(m, 2H), 4.90(dd, 1H), 4.38(m, 1H), 3.57(s, 2H), 3.30(dd, 1H), 1.70(m, 1H), 1.40(m, 1H), 1.10(m, 1H), 0.98(m, 6H)

Example 23

N-(2,3-Dichlorobenzyl)-N-(4-bromophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.20-8.40(m, 13H), 5.56(d, 2H), 5.32(m, 2H), 4.96(dd, 1H), 4.42(m, 1H), 3.58(s, 2H), 3.33(dd, 1H), 1.70(m, 1H), 1.40(m, 1H), 1.10(m, 1H), 0.98(m, 6H)

Example 24

N-(2,3-Dichlorobenzyl)-N-(2-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.90-8.20(m, 13H), 5.80(m, 1H), 5.38(m, 2H), 4.65-5.04(m, 2H), 4.50(dd, 1H), 4.05-4.38(m, 2H), 3.28(s, 2H), 3.00(dd, 1H), 1.65(m, 1H), 1.38(m, 1H), 1.05(m, 1H), 0.88(m, 6H)

Example 25

N-(2,3-Dichlorobenzyl)-N-(3-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.02-8.18(m, 13H), 5.30(m, 2H), 4.82-5.24(m, 2H), 4.62(dd, 1H), 4.18(m, 1H), 3.35(s, 2H), 3.06(dd, 1H), 1.68(m, 1H), 1.40(m, 1H), 1.00(m, 1H), 0.85(m, 6H)

Example 26

N-(2,3-Dichlorobenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-8.20(m, 12H), 5.30(m, 2H), 5.05(m, 2H), 4.70(dd, 1H), 4.22(m, 1H), 3.35(s, 2H), 3.12(dd, 1H), 1.65(m, 1H), 1.40(m, 1H), 1.00(m, 1H), 0.85(m, 6H)

Example 27

N-(2,3-Dichlorobenzyl)-N-(benzylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of N-(2,3-dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine prepared from Preparative Example 5 in methylene chloride (0.02M, 1ml, 0.02mmol) was added benzylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 2hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: methylene chloride/ methanol=9/1, v/v) to give the title compound as a white solid.

¹H-NMR (CDCl₃) : δ 6.82-7.58(m, 14H), 6.05(t, 1H), 5.22(d, 2H),

5.05(m, 1H), 4.42-4.80(m, 4H), 4.05(m, 1H), 3.20(s, 2H), 3.00(dd, 1H), 1.58(m, 1H), 1.37(m, 1H), 1.00(m, 1H), 0.82(m, 6H)

Examples 28-67

N-(2,3-Dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine was reacted with the corresponding isothiocyanates under the same condition as described in Example 27 to give the title compounds.

Example 28

N-(2,3-Dichlorobenzyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.65(m, 13H), 5.20(d, 2H), 4.62-5.10(m, 3H), 4.20(m, 1H), 3.32(s, 2H), 3.05(dd, 1H), 1.55(m, 1H), 1.38(m, 1H), 0.98(m, 1H), 0.80(m, 6H)

Example 29

N-(2,3-Dichlorobenzyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-8.20(m, 13H), 4.85-5.28(m, 4H), 4.05(d, 1H), 3.35(s, 2H), 3.10(dd, 1H), 1.65(m, 1H), 1.44(m, 1H), 0.84-1.08(m, 7H)

Example 30

N-(2,3-Dichlorobenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.90-8.00(m, 13H), 4.60-5.28(m, 5H), 4.08(m, 1H), 3.25(s, 2H), 3.05(dd, 1H), 1.60(m, 1H), 1.38(m, 1H), 0.85-1.05(m, 7H)

Example 31

N-(2,3-Dichlorobenzyl)-N-(ethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.80-7.60(m, 9H), 5.68(t, 1H), 5.22(dd, 2H), 4.98(t, 1H), 4.38-4.75(dd, 2H), 4.00(m, 1H), 3.58(m, 2H), 3.25(s, 2H), 2.88(dd, 1H), 1.58(m, 1H), 1.38(m, 1H), 1.02(t, 3H), 0.80-1.00(m, 7H)

Example 32

N-(2,3-Dichlorobenzyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.95-7.55(m, 13H), 5.02-5.25(m, 3H), 4.60-5.00(dd, 2H), 3.28(s, 2H), 3.02(dd, 1H), 1.60(m, 1H), 1.38(m, 1H), 0.85-1.05(m, 7H)

Example 33

N-(2,3-Dichlorobenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.90-8.18(m, 13H), 5.25(d, 1H), 4.88(q, 1H), 4.63, 5.20(dd, 2H), 4.15(m, 1H), 3.35(s, 2H), 3.10(dd, 1H), 1.62(m, 1H), 1.44(m, 1H), 0.85-1.05(m, 7H)

Example 34

N-(2,3-Dichlorobenzyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobe

nzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.90-7.68(m, 13H), 5.20(d, 1H), 4.85(bs, 1H), 4.60, 5.10(dd, 2H), 4.08(m, 1H), 3.25(s, 2H), 3.08(dd, 1H), 1.60(m, 1H), 1.38(m, 1H), 0.85-1.05(m, 7H)

Example 35

N-(2,3-Dichlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.82-7.60(m, 13H), 5.28(d, 1H), 4.65-5.18(m, 3H), 4.18(m, 1H), 3.78(s, 3H), 3.32(s, 2H), 3.05(dd, 1H), 1.62(m, 1H), 1.45(m, 1H), 0.85-1.10(m, 7H)

Example 36

N-(2,3-Dichlorobenzyl)-N-(methylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.90-7.65(m, 9H), 6.05(bs, 1H), 5.30(dd, 1H), 5.05(t, 1H), 4.40-4.80(dd, 2H), 4.10(m, 1H), 3.32(s, 2H), 3.10(d, 3H), 3.00(dd, 1H), 1.60(m, 1H), 1.45(m, 1H), 0.85-1.10(m, 7H)

Example 37

N-(2,3-Dichlorobenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.95-8.20(m, 13H), 4.55-5.38(m, 5H), 4.08(m, 1H), 3.28(s, 2H), 3.05(dd, 1H), 1.60(m, 1H), 1.40(m, 1H), 0.85-1.10(m, 7H)

Example 38

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.85-7.65(m, 9H), 5.92(t, 1H), 5.78(m, 1H), 5.35(d, 2H), 5.10(m, 3H), 4.42-4.78(dd, 2H), 4.25(m, 2H), 4.10(m, 1H), 3.32(s, 2H), 3.00(dd, 1H), 1.62(m, 1H), 1.44(m, 1H), 0.85-1.15(m, 7H)

Example 39

N-(2,3-Dichlorobenzyl)-N-(pyridine-4-ylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 8.2(s, 2H), 6.8-7.6(m, 11H), 5.5 (t, 1H), 5.2(m, 3H), 4.6(m, 2H), 4.1(bs, 1H), 3.4(s, 2H), 3.1(m, 1H), 0.8-1.7(m, 9H)

Example 40

N-(2,3-Dichlorobenzyl)-N-(isobutylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.65(m, 9H), 6.91(d, 1H), 5.74(bs, 1H), 5.30(m, 2H), 5.05-5.20(m, 1H), 4.62(dd, 2H), 4.05-4.13(m, 1H), 3.45-3.58(m, 1H), 3.25(m, 2H), 3.02(m, 1H), 1.83(m, 1H), 1.62(bs, 1H), 1.45(m, 1H), 1.05(m, 1H), 0.90(m, 6H), 0.75(m, 6H)

Example 41

N-(2,3-Dichlorobenzyl)-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.75-7.65(m, 9H), 5.75(bs, 1H), 5.32(d, 2H), 5.10(t, 1H), 4.60(dd, 2H), 4.08(m, 1H), 3.45(m, 2H), 3.30(s, 2H), 3.00(dd,

1H), 1.65(m, 1H), 1.45(m, 3H), 1.20(m, 2H), 1.05(m, 1H), 0.86(m, 6H)

Example 42

N-(2,3-Dichlorobenzyl)-N-(ethoxycarbonylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.65(m, 9H), 6.20(bs, 1H), 5.24-5.35(m, 3H), 4.45 & 4.76(dd, 2H), 4.18(m, 3H), 3.35(d, 2H), 3.00(dd, 1H), 1.30-1.65(m, 2H), 1.22 (t, 3H), 1.05(m, 1H), 0.82(m, 6H)

Example 43

N-(2,3-Dichlorobenzyl)-N-(1-naphthylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.95-7.80(m, 16H), 5.10-5.30(m, 4H), 4.80(d, 1H), 4.22(m, 1H), 3.32(s, 2H), 3.18(dd, 1H), 1.40-1.66(m, 2H), 1.05(m, 1H), 0.90(m, 6H)

Example 44

N-(2,3-Dichlorobenzyl)-N-(phenethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.70-7.60(m, 14H), 5.50(bs, 1H), 5.35(d, 2H), 5.08(t, 1H), 4.40(d, 2H), 4.05(m, 1H), 3.80(m, 2H), 3.30(s, 2H), 2.98(dd, 1H), 2.80 (t, 2H), 1.60(m, 1H), 1.42(m, 1H), 1.05(m, 1H), 0.90(m, 6H)

Example 45

N-(2,3-Dichlorobenzyl)-N-(benzoylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.05-7.80(m, 14H), 6.38(bs, 1H), 5.35(s, 2H), 4.70-5.20(bs, 3H), 4.30(bs, 1H), 3.45(s, 2H), 3.20(bs, 1H), 2.00(bs, 1H), 1.50(m, 1H), 1.00(m, 1H), 0.80(m, 6H)

Example 46

N-(2,3-Dichlorobenzyl)-N-(cyclohexylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.90-7.70(m, 9H), 5.38(d, 2H), 5.10 (t, 1H), 4.42-4.80(dd, 2H), 4.25(m, 1H), 4.06(m, 1H), 3.35(s, 2H), 3.00(dd, 1H), 1.05-2.00(m, 13H), 0.90(m, 6H)

Example 47

N-(2,3-Dichlorobenzyl)-N-[(4-dimethylamino)-1-naphthylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 15H), 5.08-5.28(m, 3H), 4.80(d, 1H), 4.22(m, 1H), 3.35(s, 2H), 3.17(dd, 2H), 2.85(s, 6H), 1.65(m, 1H), 1.42(m, 1H), 0.90(m, 6H)

Example 48

N-(2,3-Dichlorobenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.80-8.24(m, 13H), 5.32(m, 1H), 5.20(s, 2H), 4.62-5.00(dd, 2H), 4.22(m, 1H), 3.56(s, 3H), 3.35(s, 2H), 3.10(dd, 1H), 1.64(bs, 1H), 1.42(m, 1H), 0.92(m, 6H)

Example 49

N-(2,3-Dichlorobenzyl)-N-(4-nitrophenylthiocarbamoyl)-2(S)-{[1-(4-cyanoben

zyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.95-8.18(m, 13H), 5.42(m, 1H), 5.28(s, 2H), 4.65(d, 2H), 4.16(m, 1H), 3.38(s, 2H), 3.17(dd, 1H), 1.64(bs, 1H), 1.42(m, 1H), 0.92(m, 6H)

Example 50

N-(2,3-Dichlorobenzyl)-N-(phenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.80(m, 14H), 5.28(d, 2H), 5.02-5.18(m, 2H), 4.65(d, 1H), 4.18(bs, 1H), 3.34(s, 2H), 3.10(dd, 1H), 1.64(bs, 1H), 1.42(m, 1H), 0.94(m, 6H)

Example 51

N-(2,3-Dichlorobenzyl)-N-(n-propylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.75(m, 9H), 5.35(d, 2H), 5.10(m, 1H), 4.42-4.80(dd, 2H), 4.08(m, 1H), 3.68 (t, 2H), 3.32(s, 2H), 3.02(dd, 1H), 1.62(m, 1H), 1.50(m, 2H), 1.40(m, 1H), 1.05(m, 1H), 0.94(m, 6H), 0.78 (t, 3H)

Example 52

N-(2,3-Dichlorobenzyl)-N-(3-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.65(m, 13H), 5.30(d, 2H), 5.20(m, 1H), 4.70 & 5.04(dd, 2H), 4.20(m, 1H), 3.32(s, 2H), 3.12(dd, 1H), 2.12(s, 3H), 1.64(bs, 1H), 1.42(m, 1H), 1.05(m, 1H), 0.90(m, 6H)

Example 53

N-(2,3-Dichlorobenzyl)-N-(2-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.65(m, 13H), 5.28(d, 2H), 5.02-5.20(m, 2H), 4.65(d, 1H), 4.15(m, 1H), 3.35(s, 2H), 3.08(dd, 1H), 2.34(s, 3H), 1.36-1.70(m, 2H), 1.05(m, 1H), 0.88(m, 6H)

Example 54

N-(2,3-Dichlorobenzyl)-N-(4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.65(m, 13H), 5.30(d, 2H), 5.02-5.22(m, 2H), 4.65(d, 1H), 4.15(m, 1H), 3.32(s, 2H), 3.08(dd, 1H), 2.35(s, 3H), 1.35-1.70(m, 2H), 1.05(m, 1H), 0.88(m, 6H)

Example 55

N-(2,3-Dichlorobenzyl)-N-(4-azidophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.90(m, 13H), 5.28(d, 2H), 4.90-5.22(m, 2H), 4.62(d, 1H), 4.10(m, 1H), 3.30(s, 2H), 3.08(dd, 1H), 1.35-1.70(m, 2H), 1.05(m, 1H), 0.88(m, 6H)

Example 56

N-(2,3-Dichlorobenzyl)-N-(4-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.90-7.60(m, 13H), 5.22(d, 2H), 4.95 (t, 1H),

4.62 & 5.10(dd, 2H), 4.10(m, 1H), 3.30(s, 2H), 3.08(dd, 1H), 1.35-1.70(m, 2H), 1.05(m, 1H), 0.88(m, 6H)

Example 57

N-(2,3-Dichlorobenzyl)-N-(2-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.70(m, 13H), 5.24(s, 2H), 5.18(m, 1H), 4.74 & 5.10(dd, 2H), 4.24(m, 1H), 3.35(s, 2H), 3.10(dd, 1H), 1.62(bs, 1H), 1.42(m, 1H), 1.05(m, 1H), 0.92(m, 6H)

Example 58

N-(2,3-Dichlorobenzyl)-N-(3-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.60(m, 13H), 5.25 (s & m, 3H), 4.96(bs, 1H), 4.62(d, 1H), 4.17(m, 1H), 3.34(s, 2H), 3.10(dd, 1H), 1.62(bs, 1H), 1.42(m, 1H), 1.05(m, 1H), 0.92(m, 6H)

Example 59

N-(2,3-Dichlorobenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.65(m, 12H), 5.28(d, 2H), 5.10(bs, 2H), 4.70(d, 1H), 4.21(m, 1H), 3.35(s, 2H), 3.15(dd, 1H), 1.62(bs, 1H), 1.40(m, 1H), 1.04(m, 1H), 0.90(m, 6H)

Example 60

N-(2,3-Dichlorobenzyl)-N-(2-methoxypyridine-5-ylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-7.84(m, 12H), 6.68(d, 1H), 5.28(d, 2H), 4.98-5.20(bs, 2H), 4.68(d, 1H), 4.18(m, 1H), 3.87(s, 3H), 3.30(s, 2H), 3.12(dd, 1H), 1.40-1.62(m, 2H), 1.02(m, 1H), 0.90(m, 6H)

Example 61

N-(2,3-Dichlorobenzyl)-N-(3-ethoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.80-7.65(m, 10H), 5.38(d, 2H), 5.20(m, 1H), 4.52(d, 2H), 4.05(m, 1H), 3.70(m, 2H), 3.40(m, 2H), 3.32(s, 2H), 3.06-3.28(m, 4H), 2.93(dd, 1H), 1.75 (t, 3H), 1.60(bs, 1H), 1.40(m, 1H), 1.04(m, 1H), 0.85(m, 6H)

Example 62

N-(2,3-Dichlorobenzyl)-N-(4-aminophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.25-8.20(m, 5H), 6.92-7.25(m, 6H), 6.40-6.90(m, 3H), 4.78-5.40(m, 4H), 4.60(m, 1H), 4.07(m, 1H), 2.80-3.40(m, 3H), 1.95(m, 1H), 1.25-1.70(m, 2H), 0.90(m, 6H)

Example 63

N-(2,3-Dichlorobenzyl)-N-(2-methoxyethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.82-7.65(m, 10H), 5.95(bs, 1H), 5.38(d, 2H), 5.18(m, 1H), 4.60(dd, 2H), 4.10(m, 1H), 3.72 (t, 2H), 3.40 (t, 2H), 3.28(s, 2H), 3.15(s, 3H), 3.02(dd, 1H), 1.63(bs, 1H), 1.42(m, 1H), 1.04(m, 1H), 0.88(m, 6H)

Example 64

N-(2,3-Dichlorobenzyl)-N-(cyclopentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.80-7.65(m, 9H), 5.55(bs, 1H), 5.38(d, 2H), 5.05(m, 1H), 4.62(m, 1H), 4.42-4.78(dd, 2H), 4.06(m, 1H), 3.32(s, 2H), 3.00(dd, 1H), 2.00(m, 4H), 1.40-1.65(m, 6H), 1.05(m, 1H), 0.92(m, 6H)

Example 65

N-(2,3-Dichlorobenzyl)-N-(cyclopropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.85-7.65(m, 9H), 6.08(bs, 1H), 5.32(d, 2H), 4.88(m, 1H), 4.42-4.82(dd, 2H), 4.05(m, 1H), 3.30(s, 2H), 3.08(m, 1H), 2.98(dd, 1H), 1.38-1.64(m, 2H), 1.05(m, 1H), 0.80-0.92(m, 10H)

Example 66

N-(2,3-Dichlorobenzyl)-N-(ethoxycarbonylmethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.65(m, 9H), 6.45(bs, 1H), 5.30(d, 2H), 4.90(m, 1H), 4.50-4.88(dd, 2H), 4.35(m, 2H), 4.08(m, 3H), 3.34(s, 2H), 3.02(dd, 1H), 1.38-1.64(m, 2H), 1.22 (t, 3H), 1.05(m, 1H), 0.88(m, 6H)

Example 67

N-(2,3-Dichlorobenzyl)-N-[(4-dimethylamino)phenylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.65-7.62(m, 13H), 5.32(d, 2H), 5.20(m, 1H),

4.62-5.02(dd, 2H), 4.18(m, 1H), 3.55(s, 2H), 3.05(dd, 1H), 2.97(s, 6H), 1.38-1.65(m, 2H), 1.22 (t, 3H), 1.05(m, 1H), 0.90(m, 6H)

Example 68

N-(2,3-Dichlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyano benzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine HCl

The compound (500 mg) prepared from Example 35 was dissolved in HCl-ethanol (6N, 5ml), and stirred for 2 hr at room temperature. The reaction mixture was concentrated *in vacuo*, and the residue was crystallized from methylene chloride/diethylether(1/10, v/v) to give the title compound as a white solid.

¹H-NMR (CDCl₃) : δ 8.83(s, 1H), 7.60(d, 2H), 7.48(s, 1H), 7.34(m, 3H), 7.20(m, 1H), 7.07(d, 3H), 6.72(d, 2H), 5.50(s, 2H), 4.82-5.20(m, 2H), 3.80-4.50(m, 2H), 3.40-3.80(m, 5H), 3.20(s, 2H), 0.97-1.60(m, 3H), 0.70-0.97(m, 6H)

Example 69

N-(2,3-Dichlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyano benzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine methanesulfonic acid salt

To a solution of the compound (500 mg) prepared from Example 35 in methylene chloride (10ml) were added methanesulfonic acid (3ml) and water (0.5ml), and the resulting mixture was stirred for 30 min at room temperature. The organic phase was separated, dried over MgSO₄, and concentrated *in vacuo*. The residue was crystallized from methylene chloride / diethylether(1/10, v/v) to give the title compound as a white solid.

¹H-NMR (CDCl₃) : δ 14.9(s, 1H), 8.30-8.80(m, 2H), 7.37-7.80(m, 4H), 7.10-7.35(m, 4H), 6.82(d, 2H), 5.40-5.80(m, 3H), 4.40-4.80(m, 2H), 4.22(m, 1H), 3.80(s, 3H), 3.40-3.77(m, 2H), 3.23(m, 1H), 2.00-2.40(bs, 2H), 2.76(s, 3H), 1.10-1.90(m, 3H), 0.80-1.05(m, 6H)

Example 70

N-(2,3-Dichlorobenzyl)-N-(cyclohexylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine HCl

The compound prepared from Example 46 was reacted under the same condition as described in Example 68 to give the title compound.

¹H-NMR (CDCl₃) : δ 8.10-8.14(m, 1H), 7.70(d, 2H), 7.41-7.49(m, 5H), 7.20 (t, 1H), 7.00(d, 1H), 5.76(bs, 2H), 4.95-4.73(m, 2H), 4.06-4.25(m, 2H), 3.58(bs, 2H), 3.03-3.13(m, 1H), 1.87(bs, 2H), 1.55-1.61(m, 3H), 1.02-1.36(m, 9H), 0.91-0.94(m, 6H)

Example 71

N-(2,3-Dichlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(R)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(R)-methylpentylamine HCl

N-t-Butoxycarbonyl-D-isoleucine aldehyde was reacted under the same condition as described in Preparative Example 4 to give a compound N-(2,3-dichlorobenzyl)-2(R)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(R)-methylpentylamine, which was then reacted with 4-methoxyphenylisothiocyanate under the same condition as described in Example 27 and Example 68 to give the title compound.

¹H-NMR (CDCl₃) : δ 8.9(s, 1H), 7.2(d, 2H), 7.5(s, 1H), 7.4-7.5(m, 3H),

7.3 (t, 1H), 7.2(d, 3H), 6.8(d, 2H), 5.6(s, 2H), 5.2(dd, 2H), 4.9(s, 3H), 4.3(m, 1H), 4.2(m, 1H), 1.6-1.8 (m, 4H), 1.5-1.6(m, 2H), 1.2(m, 1H), 0.8-0.9(m, 6H)

Example 72

N-(2,3-Dichlorobenzyl)-N-(thiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

<Step 1>

N-(2,3-Dichlorobenzyl)-N-(thiocarbamoyl)-2(S)-(t-butoxycarbonyl)amino-3(S)-methylpentylamine

To a solution of N-(2,3-dichlorobenzyl)-2(S)-(t-butoxycarbonyl)amino-3(S)-methylpentylamine (2.15 g, 5.7 mmol) in methylene chloride (50 ml) was added benzoylisothiocyanate (0.93 g, 5.7 mmol), and then stirred for 2 hr at room temperature. The reaction mixture was concentrated *in vacuo*, and then the resulting residue was dissolved in methanol (50 ml) and 2N NaOH (50 ml). The reaction mixture was refluxed for 24 hr, concentrated *in vacuo*, and the residue was purified by silica gel column chromatography(eluent: methylene chloride/methanol =10/1, v/v) to give the title compound (1.15 g).

<Step 2>

N-(2,3-Dichlorobenzyl)-N-(thiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of N-(2,3-dichlorobenzyl)-N-(thiocarbamoyl)-2(S)-(t-butoxycarbonyl)amino-3(S)-methylpentylamine (90 mg, 0.21 mmol) in dichloromethane (7 ml) was added trifluoroacetic acid (3 ml), and stirred for 1 hr at room temperature. The reaction mixture was washed

with saturated sodium bicarbonate, dried over MgSO_4 , and concentrated *in vacuo*. The residue was reacted with 1-(4-cyanobenzyl)-1H-imidazol-5-yl acetic acid HCl (69 mg, 0.25 mmol) under the same condition described in <step 4> of Preparative Example 4 to give the title compound (20 mg).

$^1\text{H-NMR}$ (CDCl_3) : δ 6.88-7.65(m, 9H), 6.60(bs, 2H), 5.35 (q, 2H), 4.60-5.18(br, 2H), 4.50(dd, 1H), 4.18(m, 1H), 3.36(d, 2H), 2.98(dd, 1H), 1.06-1.65(m, 3H), 0.86(m, 6H)

Example 73

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

<Step 1>

N-(2,3-dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

Using the same method as described in Preparative Example 3, N-t-butoxycarbonyl-L-alanine was converted to N-(*t*-butoxycarbonyl)-L-alanine aldehyde. And then the reaction was carried out as described in Preparative Example 4, but replacing 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid HCl with 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid HCl to give the title compound.

$^1\text{H-NMR}$ (CDCl_3) : δ 6.99-7.62(m, 9H), 6.17(d, 1H), 5.25(s, 2H), 3.98(m, 1H), 3.85(s, 2H), 3.33(s, 2H), 2.59(d, 2H), 1.09(d, 3H)

<Step 2>

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-i

midazol-5-yl]acetyl}aminopropylamine

To a solution of N-(2,3-dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine in methylenechloride (0.02M, 1ml, 0.02mmol) was added allylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 1hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: methylene chloride/methanol=9/1, v/v) to give the title compound as a white solid.

¹H-NMR (CDCl₃) : δ 6.93-7.66(m, 9H), 6.52(bs, 1H), 5.85(m, 1H), 5.30(s, 2H), 5.15(d, 1H), 5.08(m, 2H), 4.65(bs, 1H), 4.60(d, 1H), 4.29(bs, 2H), 4.10(m, 1H), 3.32(s, 2H), 2.95(dd, 1H), 1.19(d, 3H)

Examples 74-116

N-(2,3-Dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 73 to give the title compounds.

Example 74

N-(2,3-Dichlorobenzyl)-N-(benzylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.92-7.62(m, 14H), 5.30(s, 2H), 5.26(d, 1H), 4.86(s, 2H), 4.72(bs, 1H), 4.62(d, 1H), 4.08(m, 1H), 3.25(s, 2H), 2.97(dd, 1H), 1.19(d, 3H)

Example 75

N-(2,3-Dichlorobenzyl)-N-(2-biphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl

)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.95-7.67(m, 18H), 6.69(d, 1H), 5.25(d, 1H), 5.23(s, 2H), 4.47(bs, 1H), 4.47(m, 1H), 3.94(s, 1H), 3.29(s, 2H), 2.86(dd, 1H), 1.13(d, 3H)

Example 76

N-(2,3-Dichlorobenzyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.04(bs, 1H), 6.97-7.67(m, 13H), 5.30(s, 2H), 5.28(d, 1H), 4.81(bs, 1H), 4.77(d, 1H), 4.29(m, 1H), 3.36(s, 2H), 3.07(dd, 1H), 1.21(d, 3H)

Example 77

N-(2,3-Dichlorobenzyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 9.12(bs, 1H), 6.93-7.59(m, 13H), 5.70(d, 1H), 5.30(s, 2H), 4.70(d, 1H), 4.48(m, 1H), 4.13(m, 1H), 3.33(s, 2H), 2.98(dd, 1H), 1.25(d, 3H)

Example 78

N-(2,3-Dichlorobenzyl)-N-(4-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.85(bs, 1H), 6.93-7.59(m, 13H), 5.61(d, 1H), 5.24(s, 2H), 4.71(d, 1H), 4.52(m, 1H), 4.12(m, 1H), 3.33(s, 2H), 2.98(dd, 1H), 1.24(d, 3H)

Example 79

N-(2,3-Dichlorobenzyl)-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.93-7.67(m, 9H), 6.38(bs, 1H), 5.34(s, 2H), 5.14(d, 1H), 4.70(m, 1H), 4.59(d, 1H), 4.09(m, 1H), 3.61(m, 2H), 3.33(s, 2H), 2.94(dd, 1H), 1.54(m, 2H), 1.27(m, 2H), 1.20(d, 3H), 0.89 (t, 3H)

Example 80

N-(2,3-Dichlorobenzyl)-N-(isobutylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.94-7.67(m, 9H), 6.31(bs, 1H), 5.34(s, 2H), 5.10(d, 1H), 4.76(m, 1H), 4.60(d, 1H), 4.11(m, 1H), 3.45(m, 2H), 3.32(s, 2H), 2.97(dd, 1H), 1.92(m, 1H), 1.18(d, 3H), 0.81 (t, 6H)

Example 81

N-(2,3-Dichlorobenzyl)-N-(2-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.05(bs, 1H), 6.97-7.66(m, 13H), 5.27(d, 1H), 5.25(s, 2H), 4.81(bs, 1H), 4.77(d, 1H), 4.27(m, 1H), 3.33(s, 2H), 3.07(dd, 1H), 1.21(d, 3H)

Example 82

N-(2,3-Dichlorobenzyl)-N-(3-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 9.10(bs, 1H), 6.93-7.59(m, 13H), 5.69(d, 1H), 5.28(s, 2H), 4.70(d, 1H), 4.48(m, 1H), 4.13(m, 1H), 3.33(s, 2H), 2.99(dd,

1H), 1.25(d, 3H)

Example 83

N-(2,3-Dichlorobenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.81(bs, 1H), 6.94-7.59(m, 13H), 5.60(d, 1H), 5.24(s, 2H), 4.71(d, 1H), 4.52(m, 1H), 4.13(m, 1H), 3.33(s, 2H), 2.99(dd, 1H), 1.24(d, 3H)

Example 84

N-(2,3-Dichlorobenzyl)-N-(3-chloro-4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.93(bs, 1H), 6.94-7.60(m, 12H), 5.63(d, 1H), 5.29(s, 2H), 4.71(d, 1H), 4.53(bs, 1H), 4.15(m, 1H), 3.33(s, 2H), 2.99(dd, 1H), 2.35(s, 3H), 1.25(d, 3H)

Example 85

N-(2,3-Dichlorobenzyl)-N-(cyclohexylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.91-7.66(m, 9H), 5.98(bs, 1H), 5.33(s, 2H), 5.16(d, 1H), 4.73(m, 1H), 4.58(d, 1H), 4.27(m, 1H), 4.06(m, 1H), 3.33(s, 2H), 2.92(dd, 1H), 1.93(m, 2H), 1.01-1.63(m, 8H), 1.16(d, 3H)

Example 86

N-(2,3-Dichlorobenzyl)-N-(cyclopentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.93-7.66(m, 9H), 6.21(bs, 1H), 5.33(s, 2H), 5.17(d, 1H), 4.68(m, 1H), 4.58(d, 1H), 4.05(m, 1H), 3.32(s, 2H), 2.91(dd, 1H), 2.02(m, 2H), 1.25-1.56(m, 6H), 1.18(d, 3H)

Example 87

N-(2,3-Dichlorobenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.28(bs, 1H), 6.94-7.62(m, 12H), 5.27(d, 1H), 5.24(s, 2H), 4.75(d, 1H), 4.71(m, 1H), 4.25(m, 1H), 3.32(s, 2H), 3.06(dd, 1H), 1.21(d, 3H)

Example 88

N-(2,3-Dichlorobenzyl)-N-[2-(dimethylamino)ethylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.98-7.66(m, 9H), 5.41(d, 1H), 5.29(s, 2H), 4.90(m, 1H), 4.64(d, 1H), 4.20(m, 1H), 3.59(m, 2H), 3.28(dd, 2H), 3.12(dd, 1H), 2.54(m, 2H), 2.10(s, 6H), 1.17(d, 3H)

Example 89

N-(2,3-Dichlorobenzyl)-N-[4-(dimethylamino)phenylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 7.96(bs, 1H), 6.63-7.60(m, 13H), 5.29(s, 2H), 5.20(d, 1H), 4.86(m, 1H), 4.73(d, 1H), 4.18(m, 1H), 3.32(s, 2H), 3.02(dd, 1H), 2.95(s, 6H), 1.20(d, 3H)

Example 90

N-(2,3-Dichlorobenzyl)-N-[3-(dimethylamino)propylthiocarbamoyl]-2(S)-{[1-(

4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.91(bs, 1H), 6.80-7.66(m, 9H), 5.44(d, 1H), 5.36(s, 2H), 4.95(m, 1H), 4.55(d, 2H), 4.12(m, 1H), 3.68(m, 2H), 3.32(dd, 2H), 2.92(dd, 1H), 2.41(m, 2H), 1.72(m, 2H), 1.90(s, 6H), 1.13(d, 3H)

Example 91

N-(2,3-Dichlorobenzyl)-N-(3-ethoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 7.75(bs, 1H), 6.84-7.67(m, 9H), 5.35(s, 2H), 4.94(t, 1H), 4.66(dd, 2H), 4.12(m, 1H), 3.74(bs, 2H), 3.42(m, 2H), 3.32(s, 2H), 3.21(m, 2H), 2.94(dd, 1H), 1.78(bs, 2H), 1.14(d, 3H), 0.90 (t, 3H)

Example 92

N-(2,3-Dichlorobenzyl)-N-(ethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.92-7.66(m, 9H), 6.45(bs, 1H), 5.34(s, 2H), 5.18(d, 1H), 4.63(m, 1H), 4.58(d, 1H), 4.07(m, 1H), 3.66(m, 2H), 3.32(s, 2H), 2.91(dd, 1H), 1.18(d, 3H), 1.16 (t, 3H)

Example 93

N-(2,3-Dichlorobenzyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.28(bs, 1H), 6.95-7.60(m, 13H), 5.36(d, 1H), 5.25(s, 2H), 4.79(m, 1H), 4.75(d, 1H), 4.22(m, 1H), 3.32(s, 2H), 3.04(dd, 1H), 1.21(d, 3H)

Example 94

N-(2,3-Dichlorobenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.98(bs, 1H), 6.86-7.59(m, 13H), 5.66(d, 1H), 5.26(s, 2H), 4.70(d, 1H), 4.52(m, 1H), 4.13(m, 1H), 3.33(s, 2H), 2.99(dd, 1H), 1.25(d, 3H)

Example 95

N-(2,3-Dichlorobenzyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.56(bs, 1H), 6.96-7.60(m, 13H), 5.52(d, 1H), 5.26(s, 2H), 4.72(d, 1H), 4.59(m, 1H), 4.14(m, 1H), 3.32(s, 2H), 3.00(dd, 1H), 1.23(d, 3H)

Example 96

N-(2,3-Dichlorobenzyl)-N-(4-hydroxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CD₃OD) : δ 6.69-7.75(m, 13H), 5.37(s, 2H), 5.32(d, 1H), 5.00(d, 1H), 4.24(m, 1H), 4.10(m, 1H), 3.43(dd, 1H), 3.41(s, 2H), 1.17(d, 3H)

Example 97

N-(2,3-Dichlorobenzyl)-N-(4-isopropylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.22(bs, 1H), 6.98-7.59(m, 13H), 5.39(d, 1H),

5.26(s, 2H), 4.76(m, 1H), 4.72(d, 1H), 4.17(m, 1H), 3.32(s, 2H), 3.01(dd, 1H), 2.90(m, 1H), 1.23(d, 9H)

Example 98

N-(2,3-Dichlorobenzyl)-N-(2-methoxyethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.88-7.66(m, 9H), 6.26(bs, 1H), 5.34(s, 2H), 4.91(d, 1H), 4.86 (t, 1H), 4.61(d, 2H), 4.13(m, 1H), 3.78(m, 2H), 3.44(m, 2H), 3.32(s, 2H), 3.17(s, 3H), 3.02(dd, 1H), 1.16(d, 3H)

Example 99

N-(2,3-Dichlorobenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.18(d, 1H), 6.79-7.62(m, 13H), 5.23(s, 2H), 5.11(m, 1H), 5.01(d, 1H), 4.76(d, 1H), 4.30(m, 1H), 3.60(s, 3H), 3.35(s, 2H), 3.12(dd, 1H), 1.20(d, 3H)

Example 100

N-(2,3-Dichlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.26(bs, 1H), 6.84-7.59(m, 13H), 5.38(d, 1H), 5.26(s, 2H), 4.75(m, 1H), 4.72(d, 1H), 4.16(m, 1H), 3.79(s, 3H), 3.31(s, 2H), 3.01(dd, 1H), 1.21(d, 3H)

Example 101

N-(2,3-Dichlorobenzyl)-N-(3-methoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 7.82(bs, 1H), 6.81-7.67(m, 9H), 5.36(dd, 2H), 4.98 (t, 1H), 4.62(dd, 2H), 4.13(m, 1H), 3.68(m, 2H), 3.37(m, 2H), 3.31(s, 2H), 2.96(dd, 1H), 2.91(s, 3H), 1.76(m, 2H), 1.14(d, 3H)

Example 102

N-(2,3-Dichlorobenzyl)-N-(2-methoxypyridin-5-ylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.80(bs, 1H), 6.71-7.97(m, 12H), 5.59(d, 1H), 5.26(s, 2H), 4.73(d, 1H), 4.60(m, 1H), 4.16(m, 1H), 3.91(s, 3H), 3.32(s, 2H), 3.01(dd, 1H), 1.24(d, 3H)

Example 103

N-(2,3-Dichlorobenzyl)-N-(methylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.92-7.67(m, 9H), 6.56(bs, 1H), 5.29(s, 2H), 5.13(d, 1H), 4.65(m, 1H), 4.58(d, 1H), 4.09(m, 1H), 3.32(s, 2H), 3.11(s, 3H), 2.92(dd, 1H), 1.18(d, 3H)

Example 104

N-(2,3-Dichlorobenzyl)-N-(4-methylthiophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.59(bs, 1H), 6.94-7.59(m, 13H), 5.50(d, 1H), 5.24(s, 2H), 4.71(d, 1H), 4.61(m, 1H), 4.14(m, 1H), 3.31(s, 2H), 2.99(dd, 1H), 2.46(s, 3H), 1.22(d, 3H)

Example 105

N-(2,3-Dichlorobenzyl)-N-(2-naphthylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.89(bs, 1H), 6.96-7.81(m, 16H), 5.57(d, 1H), 5.19(s, 2H), 4.74(d, 1H), 4.62(m, 1H), 4.19(m, 1H), 3.32(s, 2H), 3.00(dd, 1H), 1.22(d, 3H)

Example 106

N-(2,3-Dichlorobenzyl)-N-(4-nitrophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 9.54(bs, 1H), 6.64-8.19(m, 13H), 5.86(d, 1H), 5.25(s, 2H), 4.72(d, 1H), 4.19(d, 1H), 4.09(m, 1H), 3.39(s, 2H), 3.00(dd, 1H), 1.29(d, 3H)

Example 107

N-(2,3-Dichlorobenzyl)-N-(n-pentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.93-7.66(m, 9H), 6.21(bs, 1H), 5.33(s, 2H), 5.07(d, 1H), 4.77(m, 1H), 4.59(d, 1H), 4.12(m, 1H), 3.63(m, 1H), 3.48(t, 2H), 3.31(s, 1H), 2.97(dd, 1H), 1.68(m, 1H), 1.17(d, 3H), 0.74-1.30(m, 8H)

Example 108

N-(2,3-Dichlorobenzyl)-N-(phenethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.73-7.65(m, 14H), 5.99(bs, 1H), 5.30(s, 2H), 4.80(d, 1H), 4.75(m, 1H), 4.45(d, 1H), 4.05(m, 1H), 3.85(m, 2H), 3.30(s,

2H), 2.92(dd, 1H), 2.84 (t, 2H), 1.14(d, 3H)

Example 109

N-(2,3-Dichlorobenzyl)-N-(phenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.51(bs, 1H), 6.95-7.57(m, 14H), 5.48(d, 1H), 5.25(s, 2H), 4.72(d, 1H), 4.68(m, 1H), 4.17(m, 1H), 3.32(s, 2H), 3.00(dd, 1H), 1.22(d, 3H)

Example 110

N-(2,3-Dichlorobenzyl)-N-(n-propylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.93-7.67(m, 9H), 6.35(bs, 1H), 5.33(s, 2H), 5.14(d, 1H), 4.72(m, 1H), 4.59(d, 1H), 4.09(m, 1H), 3.59(m, 2H), 3.33(s, 2H), 2.93(dd, 1H), 1.58(dd, 2H), 1.25(m, 2H), 1.18(d, 3H), 0.85 (t, 3H)

Example 111

N-(2,3-Dichlorobenzyl)-N-(3-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.28(bs, 1H), 6.98-7.56(m, 13H), 5.44(d, 1H), 5.26(s, 2H), 4.72(d, 1H), 4.71(m, 1H), 4.17(m, 1H), 3.33(s, 2H), 3.01(dd, 1H), 2.33(s, 3H), 1.22(d, 3H)

Example 112

N-(2,3-Dichlorobenzyl)-N-(2-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 7.87(bs, 1H), 6.96-7.60(m, 13H), 5.31(d, 1H), 5.27(s, 2H), 4.81(m, 1H), 4.75(d, 1H), 4.20(m, 1H), 3.31(s, 2H), 3.06(dd, 1H), 2.11(s, 3H), 1.20(d, 3H)

Example 113

N-(2,3-Dichlorobenzyl)-N-(4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.29(bs, 1H), 6.96-7.58(m, 13H), 5.43(d, 1H), 5.26(s, 2H), 4.72(d, 1H), 4.70(m, 1H), 4.17(m, 1H), 3.32(s, 2H), 3.00(dd, 1H), 2.33(s, 3H), 1.21(d, 3H)

Example 114

N-(2,3-Dichlorobenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 9.44(bs, 1H), 6.92-7.85(m, 13H), 5.81(d, 1H), 5.27(s, 2H), 4.71(d, 1H), 4.43(m, 1H), 4.13(m, 1H), 3.33(s, 2H), 3.00(dd, 1H), 1.28(d, 3H)

Example 115

N-(2,3-Dichlorobenzyl)-N-(2,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 7.85(bs, 1H), 6.96-7.60(m, 12H), 5.27(s, 2H), 5.20(d, 1H), 4.85(m, 1H), 4.74(d, 1H), 4.20(m, 1H), 3.31(s, 2H), 3.05(dd, 1H), 2.31(s, 3H), 2.07(s, 3H), 1.20(d, 3H)

Example 116

N-(2,3-Dichlorobenzyl)-N-(3,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cya

nobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.20(bs, 1H), 6.98-7.60(m, 12H), 5.38(d, 1H), 5.26(s, 2H), 4.74(m, 1H), 4.72(d, 1H), 4.17(m, 1H), 3.32(s, 2H), 3.01(dd, 1H), 2.22(s, 6H), 1.21(d, 3H)

Example 117

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

<Step 1>

N-(2,3-dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

Using the same method as described in Preparative Example 3, N-t-butoxycarbonyl-L-valine was converted to N-(*t*-butoxycarbonyl)-L-valine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid HCl with 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid HCl to give the title compound.

¹H-NMR (CDCl₃) : δ 7.01-7.62(m, 9H), 6.10(d, 1H), 5.26(s, 2H), 3.83(s, 2H), 3.80(m, 1H), 3.37(s, 2H), 2.64(d, 2H), 1.74(m, 1H), 0.83 (t, 6H)

<Step 2>

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

To a solution of N-(2,3-dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-

1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine in methylene chloride (0.02M, 1ml, 0.02mmol) was added allylthiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 1hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: methylene chloride/methanol=9/1, v/v) to give the title compound as a white solid.

¹H-NMR (CDCl₃) : δ 6.89-7.66(m, 9H), 6.02(bs, 1H), 5.79(m, 1H), 4.98-5.09(m, 2H), 4.80(d, 1H), 4.52(d, 1H), 4.27(m, 2H), 4.05(m, 1H), 3.32(s, 2H), 3.03(dd, 1H), 1.79(m, 1H), 0.90(d, 6H)

Examples 118-160

N-(2,3-Dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl} amino-3-methylbutylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 117 to give the title compounds.

Example 118

N-(2,3-Dichlorobenzyl)-N-(benzylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine(YHS98-18-02)

¹H-NMR(CDCl₃) : δ 6.91-7.64(m, 14H), 6.31(bs, 1H), 5.26(d, 2H), 5.07(t, 1H), 4.81(m, 2H), 4.54(d, 1H), 4.06(m, 1H), 3.26(s, 2H), 3.05(dd, 1H), 1.83(m, 1H), 1.90(d, 6H)

Example 119

N-(2,3-Dichlorobenzyl)-N-(2-biphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.64-7.75(m, 18H), 5.26(s, 2H), 4.84(m, 1H), 4.80(d, 1H), 4.48(d, 1H), 4.03(m, 1H), 3.34(s, 2H), 2.98(dd, 1H), 1.82(m, 1H), 0.87(dd, 6H)

Example 120

N-(2,3-Dichlorobenzyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.93-7.72(m, 13H), 5.24(s, 2H), 5.13(d, 1H), 5.12(m, 1H), 4.73(d, 1H), 4.20(m, 1H), 3.36(s, 2H), 3.14(dd, 1H), 1.86(m, 1H), 0.91(dd, 6H)

Example 121

N-(2,3-Dichlorobenzyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.28(bs, 1H), 6.85-7.60(m, 13H), 5.26(d, 1H), 5.24(d, 2H), 4.88(t, 1H), 4.65(d, 1H), 4.08(m, 1H), 3.32(s, 2H), 3.10(dd, 1H), 1.88(m, 1H), 0.91(t, 6H)

Example 122

N-(2,3-Dichlorobenzyl)-N-(4-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.48(bs, 1H), 6.88-7.60(m, 13H), 5.33(d, 1H), 5.26(s, 2H), 4.84(t, 1H), 4.66(d, 1H), 4.09(m, 1H), 3.34(s, 2H), 3.11(dd, 1H), 1.91(m, 1H), 0.92(dd, 6H)

Example 123

N-(2,3-Dichlorobenzyl)-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1

H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.89-7.67(m, 9H), 5.93(bs, 1H), 5.35(d, 2H), 5.04(t, 1H), 4.65(dd, 2H), 4.04(m, 1H), 3.68(m, 1H), 3.48(m, 1H), 3.33(s, 2H), 3.02(dd, 1H), 1.84(m, 1H), 1.47(m, 2H), 1.18(m, 2H), 0.89(m, 6H), 0.85(t, 3H)

Example 124

N-(2,3-Dichlorobenzyl)-N-(isobutylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.90-7.66(m, 9H), 5.91(bs, 1H), 5.35(d, 2H), 5.07(t, 1H), 4.64(dd, 2H), 4.04(m, 1H), 3.52(m, 1H), 3.32(s, 2H), 3.24(m, 1H), 3.03(dd, 1H), 1.83(m, 2H), 0.91(m, 6H), 0.75(t, 6H)

Example 125

N-(2,3-Dichlorobenzyl)-N-(2-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.94-7.69(m, 13H), 5.25(s, 2H), 5.11(d, 1H), 5.07(m, 1H), 4.72(d, 1H), 4.19(m, 1H), 3.36(s, 2H), 3.14(dd, 1H), 1.85(m, 1H), 0.91(m, 6H)

Example 126

N-(2,3-Dichlorobenzyl)-N-(3-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.47(bs, 1H), 6.89-7.60(m, 13H), 5.34(d, 1H), 5.26(s, 2H), 4.58(t, 1H), 4.66(d, 1H), 4.09(m, 1H), 3.33(s, 2H), 3.11(dd, 1H), 1.89(m, 1H), 0.92(m, 6H)

Example 127

N-(2,3-Dichlorobenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.33(bs, 1H), 6.90-7.61(m, 13H), 5.30(d, 1H), 5.24(s, 2H), 4.89(t, 1H), 4.66(d, 1H), 4.08(m, 1H), 3.32(s, 2H), 3.11(dd, 1H), 1.88(m, 1H), 0.91(t, 6H)

Example 128

N-(2,3-Dichlorobenzyl)-N-(3-chloro-4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.33(bs, 1H), 6.97-7.60(m, 12H), 5.29(d, 1H), 5.26(s, 2H), 4.89(t, 1H), 4.65(d, 1H), 4.09(m, 1H), 3.33(s, 2H), 3.10(dd, 1H), 2.32(s, 3H), 1.88(m, 1H), 0.91(t, 6H)

Example 129

N-(2,3-Dichlorobenzyl)-N-(cyclohexylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.88-7.66(m, 9H), 5.98(bs, 1H), 5.34(d, 2H), 5.06(t, 1H), 4.64(dd, 1H), 4.25(m, 1H), 4.01(m, 1H), 3.33(s, 2H), 3.00(dd, 1H), 1.84(m, 1H), 0.88-1.98(m, 10H), 0.91(t, 6H)

Example 130

N-(2,3-Dichlorobenzyl)-N-(cyclopentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.88-7.66(m, 9H), 6.25(d, 1H), 5.34(d, 2H), 5.03(t,

1H), 4.65(dd, 1H), 4.65(dd, 1H), 4.02(m, 1H), 3.33(s, 2H), 3.01(dd, 1H), 1.84(m, 1H), 1.18-2.06(m, 8H), 0.90(dd, 6H)

Example 131

N-(2,3-Dichlorobenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 7.81(bs, 1H), 6.84-7.63(m, 12H), 5.25(s, 2H), 5.14(d, 1H), 5.01(t, 1H), 4.71(d, 1H), 4.17(m, 1H), 3.34(s, 2H), 3.15(dd, 1H), 1.83(m, 1H), 0.90(t, 6H)

Example 132

N-(2,3-Dichlorobenzyl)-N-[2-(dimethylamino)ethylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 6.91-7.68(m, 9H), 6.76(bs, 1H), 5.39(dd, 2H), 5.08(t, 1H), 4.65(dd, 2H), 4.08(m, 1H), 3.53(m, 2H), 3.35(s, 2H), 3.14(dd, 1H), 2.53(m, 2H), 2.00(s, 6H), 1.88(m, 1H), 0.93(d, 6H)

Example 133

N-(2,3-Dichlorobenzyl)-N-[4-(dimethylamino)phenylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 6.60-7.61(m, 13H), 5.28(s, 2H), 5.13(t, 1H), 5.03(d, 1H), 4.66(d, 1H), 4.09(m, 1H), 3.33(s, 2H), 3.08(dd, 1H), 2.93(s, 6H), 1.85(m, 1H), 0.91(dd, 6H)

Example 134

N-(2,3-Dichlorobenzyl)-N-[3-(dimethylamino)propylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.88(bs, 1H), 6.81-7.67(m, 9H), 5.40(dd, 2H), 5.11(t, 1H), 4.52(s, 2H), 4.05(m, 1H), 3.67(m, 2H), 3.33(dd, 2H), 2.93(dd, 1H), 2.40(m, 2H), 1.87(s, 6H), 1.83(m, 1H), 1.77(m, 2H), 0.90(d, 6H)

Example 135

N-(2,3-Dichlorobenzyl)-N-(3-ethoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.76-7.67(m, 9H), 5.37(dd, 2H), 5.15(t, 1H), 4.54(d, 2H), 4.03(m, 1H), 3.72(m, 2H), 3.43(m, 2H), 3.33(s, 2H), 3.18(m, 2H), 2.93(dd, 1H), 1.78(m, 1H), 1.75(m, 2H), 0.88(m, 6H), 0.86(t, 3H)

Example 136

N-(2,3-Dichlorobenzyl)-N-(ethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.87-7.66(m, 9H), 5.94(bs, 1H), 5.34(dd, 2H), 5.00(t, 1H), 4.65(dd, 2H), 4.02(m, 1H), 3.63(m, 2H), 3.32(s, 2H), 3.00(dd, 1H), 1.84(m, 1H), 1.10(t, 3H), 0.91(m, 6H)

Example 137

N-(2,3-Dichlorobenzyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.90-7.62(m, 13H), 5.26(s, 2H), 5.11(d, 1H), 5.07(t, 1H), 4.70(d, 1H), 4.15(m, 1H), 3.36(s, 2H), 3.11(dd, 1H), 1.85(m, 1H), 0.91(dd, 6H)

Example 138

N-(2,3-Dichlorobenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 8.21(bs, 1H), 6.82-7.61(m, 13H), 5.30(d, 1H), 5.26(s, 2H), 4.89(t, 1H), 4.66(d, 1H), 4.09(m, 1H), 3.34(s, 2H), 3.11(dd, 1H), 1.87(m, 1H), 0.92(dd, 6H)

Example 139

N-(2,3-Dichlorobenzyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 8.10(bs, 1H), 6.97-7.63(m, 13H), 5.31(s, 2H), 5.22(d, 1H), 4.95(t, 1H), 4.68(d, 1H), 4.10(m, 1H), 3.34(s, 2H), 3.13(dd, 1H), 1.89(m, 1H), 0.92(dd, 6H)

Example 140

N-(2,3-Dichlorobenzyl)-N-(4-hydroxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CD₃OD) : δ 6.67-7.71(m, 13H), 5.39(s, 2H), 5.03(dd, 2H), 4.29(m, 1H), 3.87(m, 1H), 3.67(d, 1H), 3.44(s, 3H), 3.31(s, 2H), 2.68(m, 1H), 1.77(m, 1H), 0.89(t, 6H)

Example 141

N-(2,3-Dichlorobenzyl)-N-(4-isopropylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 7.02-7.77(m, 13H), 5.27(s, 2H), 5.12(d, 1H), 5.08(t, 1H), 4.67(d, 1H), 4.11(m, 1H), 3.35(s, 2H), 3.11(dd, 1H), 2.89(m, 1H),

1.86(m, 1H), 1.23(d, 6H), 0.92(dd, 6H)

Example 142

N-(2,3-Dichlorobenzyl)-N-(2-methoxyethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.88-7.66(m, 9H), 6.01(bs, 1H), 5.35(d, 2H), 5.16(1, 1H), 4.62(dd, 1H), 4.07(m, 1H), 3.82(m, 1H), 3.68(m, 1H), 3.41(m, 2H), 3.33(s, 2H), 3.13(s, 3H), 3.06(dd, 1H), 1.83(m, 1H), 0.91(d, 6H)

Example 143

N-(2,3-Dichlorobenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.27(d, 1H), 6.77-7.58(m, 13H), 5.26(m, 1H), 5.19(s, 2H), 4.82(dd, 2H), 4.18(m, 1H), 3.57(s, 3H), 3.36(s, 2H), 3.12(dd, 1H), 1.83(m, 1H), 0.93(d, 6H)

Example 144

N-(2,3-Dichlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.80(bs, 1H), 6.81-7.61(m, 13H), 5.27(dd, 2H), 5.11(m, 1H), 5.10(d, 1H), 4.66(d, 1H), 4.09(m, 1H), 3.78(s, 3H), 3.32(s, 2H), 3.09(dd, 1H), 1.86(m, 1H), 0.90(t, 6H)

Example 145

N-(2,3-Dichlorobenzyl)-N-(3-methoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.81-7.67(m, 9H), 5.37(dd, 2H), 5.17(t, 1H), 4.52(dd, 2H), 4.04(m, 1H), 3.42(m, 2H), 3.32(s, 2H), 3.29(m, 2H), 2.96(dd, 1H), 2.88(s, 3H), 1.83(m, 1H), 1.75(m, 2H), 0.90(d, 6H)

Example 146

N-(2,3-Dichlorobenzyl)-N-(2-methoxypyridin-5-ylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.35(bs, 1H), 6.66-7.89(m, 12H), 5.26(d, 2H), 5.24(d, 1H), 4.95(t, 1H), 4.67(d, 1H), 3.87(s, 3H), 3.30(s, 2H), 3.12(dd, 1H), 1.88(m, 1H), 0.91(t, 6H)

Example 147

N-(2,3-Dichlorobenzyl)-N-(methylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.88-7.68(m, 9H), 6.25(bs, 1H), 5.36(dd, 2H), 4.99(t, 1H), 4.64(dd, 2H), 4.04(m, 1H), 3.33(s, 2H), 3.08(s, 3H), 3.01(dd, 1H), 1.85(m, 1H), 0.92(dd, 6H)

Example 148

N-(2,3-Dichlorobenzyl)-N-(4-methylthiophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.10(bs, 1H), 6.96-7.60(m, 13H), 5.25(d, 2H), 5.19(d, 1H), 4.98(t, 1H), 4.66(d, 1H), 4.08(m, 1H), 3.32(s, 2H), 3.10(dd, 1H), 2.45(s, 3H), 1.87(m, 1H), 0.91(t, 6H)

Example 149

N-(2,3-Dichlorobenzyl)-N-(2-naphthylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.37(bs, 1H), 6.94-7.81(m, 16H), 5.19(d, 1H), 5.17(d, 2H), 5.01(t, 1H), 4.71(d, 1H), 4.12(m, 1H), 3.34(s, 2H), 3.11(dd, 1H), 1.87(m, 1H), 0.91(t, 6H)

Example 150

N-(2,3-Dichlorobenzyl)-N-(4-nitrophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 9.24(bs, 1H), 6.79-8.15(m, 13H), 5.54(d, 1H), 5.27(s, 2H), 4.67(d, 1H), 4.65(m, 1H), 4.08(m, 1H), 3.38(s, 2H), 3.18(dd, 1H), 1.95(m, 1H), 0.93(t, 6H)

Example 151

N-(2,3-Dichlorobenzyl)-N-(n-pentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.90-7.66(m, 9H), 5.78(bs, 1H), 5.35(dd, 2H), 5.09(t, 1H), 4.63(dd, 2H), 4.05(m, 1H), 3.32(s, 2H), 3.19-3.74(m, 2H), 3.04(dd, 1H), 1.84(m, 1H), 1.60(m, 1H), 1.16(m, 1H), 1.06(m, 2H), 0.91(dd, 6H), 0.81(m, 2H), 0.71(t, 3H)

Example 152

N-(2,3-Dichlorobenzyl)-N-(phenethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.68-7.64(m, 14H), 5.60(bs, 1H), 5.33(dd, 2H), 5.03(t, 1H), 4.44(dd, 2H), 4.00(m, 1H), 3.84(m, 2H), 3.31(s, 2H),

2.97(dd, 1H), 2.80(t, 2H), 1.81(m, 1H), 0.89(d, 6H)

Example 153

N-(2,3-Dichlorobenzyl)-N-(phenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 8.32(bs, 1H), 6.94-7.58(m, 14H), 5.23(s, 1H), 5.20(d, 1H), 5.07(t, 1H), 4.67(d, 1H), 4.10(m, 1H), 3.31(s, 2H), 3.13(dd, 1H), 1.86(m, 1H), 0.91(dd, 6H)

Example 154

N-(2,3-Dichlorobenzyl)-N-(n-propylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 6.88-7.66(m, 9H), 5.89(bs, 1H), 5.35(dd, 2H), 5.04(t, 1H), 4.64(dd, 2H), 4.03(m, 1H), 3.63(m, 1H), 3.47(m, 1H), 3.32(s, 2H), 3.01(dd, 1H), 1.84(m, 1H), 1.51(m, 2H), 0.91(m, 6H), 0.79(t, 3H)

Example 155

N-(2,3-Dichlorobenzyl)-N-(3-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 7.83(bs, 1H), 7.01-7.59(m, 13H), 5.25(s, 2H), 5.14(d, 1H), 5.02(t, 1H), 4.67(d, 1H), 4.10(m, 1H), 3.35(s, 2H), 3.10(dd, 1H), 2.31(s, 3H), 1.87(m, 1H), 0.91(dd, 6H)

Example 156

N-(2,3-Dichlorobenzyl)-N-(2-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.99-7.62(m, 13H), 5.28(s, 2H), 5.13(t, 1H), 5.08(d, 1H), 4.70(d, 1H), 4.13(m, 1H), 3.33(s, 2H), 3.13(dd, 1H), 2.05(s, 3H), 1.87(m, 1H), 0.90(dd, 6H)

Example 157

N-(2,3-Dichlorobenzyl)-N-(4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.97(bs, 1H), 6.95-7.60(m, 13H), 5.25(s, 2H), 5.14(d, 1H), 5.05(t, 1H), 4.66(d, 1H), 4.09(m, 1H), 3.32(s, 2H), 3.16(dd, 1H), 2.32(s, 3H), 1.86(m, 1H), 0.90(t, 6H)

Example 158

N-(2,3-Dichlorobenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.81(bs, 1H), 6.87-7.64(m, 13H), 5.47(d, 1H), 5.25(s, 2H), 4.71(m, 1H), 4.66(d, 1H), 4.09(m, 1H), 3.34(s, 2H), 3.14(dd, 1H), 1.92(m, 1H), 0.93(dd, 6H)

Example 159

N-(2,3-Dichlorobenzyl)-N-(2,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.89-7.62(m, 13H), 5.28(s, 2H), 5.11(t, 1H), 5.06(d, 1H), 4.69(d, 1H), 4.12(m, 1H), 3.34(s, 2H), 3.12(dd, 1H), 2.30(s, 3H), 2.01(s, 3H), 1.85(m, 1H), 0.90(dd, 6H)

Example 160

N-(2,3-Dichlorobenzyl)-N-(3,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cya

nobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.91-7.72(m, 13H), 5.27(s, 2H), 5.11(d, 1H), 5.06(t, 1H), 4.66(d, 1H), 4.10(m, 1H), 3.35(s, 2H), 3.09(dd, 1H), 2.20(s, 6H), 1.86(m, 1H), 0.91(dd, 6H)

Example 161

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

<Step 1>

N-(2,3-Dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

Using the same method as described in Preparative Example 3, N-(*t*-butoxycarbonyl)-L-leucine was converted to N-(*t*-butoxycarbonyl)-L-leucine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid HCl with 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid HCl to give the title compound.

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.99-7.63(m, 9H), 6.17(d, 1H), 5.27(s, 2H), 4.08(m, 1H), 3.85(s, 2H), 3.35(s, 2H), 2.61(d, 2H), 1.52(m, 1H), 1.27(m, 2H), 0.88(d, 6H)

<Step 2>

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

To a solution of N-(2,3-dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-

1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine in methylene chloride (0.02M, 1ml, 0.02mmol) was added allylthiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 1hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: methylene chloride/methanol=9/1, v/v) to give the title compound as a white solid.

¹H-NMR (CDCl₃) δ: 6.95-7.68(m, 9H), 6.48(bs, 1H), 5.82(m, 1H), 5.31(m, 3H), 5.05(m, 2H), 4.62(m, 2H), 4.26(m, 3H), 3.31(s, 2H), 3.01(dd, 1H), 1.25-1.53(m, 3H), 0.87(d, 6H)

Examples 162-204

N-(2,3-Dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 161 to give the title compounds.

Example 162

N-(2,3-Dichlorobenzyl)-N-(benzylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.78-7.62(m, 14H), 4.57-5.29(m, 7H), 4.21(m, 1H), 3.24(s, 2H), 3.01(dd, 1H), 1.25-1.56(m, 3H), 0.86(dd, 6H)

Example 163

N-(2,3-Dichlorobenzyl)-N-(2-biphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.65-7.72(m, 19H), 5.21(s, 2H), 5.01(d, 1H),

4.55(m, 2H), 4.15(m, 1H), 3.31(s, 2H), 2.94(dd, 1H), 1.25-1.51(m, 3H), 0.85(d, 6H)

Example 164

N-(2,3-Dichlorobenzyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.98(bs, 1H), 6.65-7.71(m, 13H), 5.32(m, 3H), 4.79(m, 2H), 4.38(m, 1H), 3.35(s, 2H), 3.09(dd, 1H), 1.25-1.54(m, 3H), 0.89(d, 6H)

Example 165

N-(2,3-Dichlorobenzyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 8.91(bs, 1H), 6.75-7.59(m, 13H), 5.53(d, 1H), 5.25(s, 2H), 4.75(d, 1H), 4.51(m, 1H), 4.18(m, 1H), 3.35(s, 2H), 3.04(dd, 1H), 1.25-1.55(m, 3H), 0.88(dd, 6H)

Example 166

N-(2,3-Dichlorobenzyl)-N-(4-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 8.67(bs, 1H), 6.67-7.61(m, 13H), 5.48(d, 1H), 5.22(s, 2H), 4.75(d, 1H), 4.52(m, 1H), 4.19(m, 1H), 3.33(s, 2H), 3.04(dd, 1H), 1.26-1.52(m, 3H), 0.88(dd, 6H)

Example 167

N-(2,3-Dichlorobenzyl)-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.84-7.66(m, 9H), 6.24(bs, 1H), 5.31(q, 2H), 5.02(d, 1H), 4.62(m, 2H), 4.16(m, 1H), 3.69(m, 1H), 3.52(m, 1H) 3.32(s, 2H), 2.96(dd, 1H), 1.16-1.58(m, 7H), 0.87(m, 9H)

Example 168

N-(2,3-Dichlorobenzyl)-N-(isobutylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.88-7.67(m, 9H), 6.24(bs, 1H), 5.31(q, 2H), 5.02(d, 1H), 4.69(m, 2H), 4.19(m, 1H), 3.55(m, 1H), 3.32(m, 3H), 3.01(dd, 1H), 1.87(m, 1H), 1.27-1.58(m, 3H), 0.83(m, 12H)

Example 169

N-(2,3-Dichlorobenzyl)-N-(2-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.93(bs, 1H), 6.63-7.68(m, 13H), 5.22(m, 3H), 4.78(m, 2H), 4.37(m, 1H), 3.35(s, 2H), 3.11(dd, 1H), 1.25-1.54(m, 3H), 0.91(d, 6H)

Example 170

N-(2,3-Dichlorobenzyl)-N-(3-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.93(bs, 1H), 6.63-7.68(m, 13H), 5.22(m, 3H), 4.78(m, 2H), 4.37(m, 1H), 3.35(s, 2H), 3.11(dd, 1H), 1.25-1.54(m, 3H), 0.91(d, 6H)

Example 171

N-(2,3-Dichlorobenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 8.69(bs, 1H), 6.72-7.61(m, 13H), 5.48(d, 1H), 5.22(s, 2H), 4.76(d, 1H), 4.55(m, 1H), 4.21(m, 1H), 3.33(s, 2H), 3.05(dd, 1H), 1.25-1.54(m, 3H), 0.88(dd, 6H)

Example 172

N-(2,3-Dichlorobenzyl)-N-(3-chloro-4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 8.69(bs, 1H), 6.78-7.61(m, 12H), 5.48(d, 1H), 5.26(s, 2H), 4.76(d, 1H), 4.55(m, 1H), 4.21(m, 1H), 3.35(s, 2H), 3.05(dd, 1H), 2.34(s, 3H), 1.26-1.54(m, 3H), 0.88(dd, 6H)

Example 173

N-(2,3-Dichlorobenzyl)-N-(cyclohexylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.81-7.67(m, 9H), 5.87(bs, 1H), 5.31(s, 2H), 5.05(d, 1H), 4.62(m, 2H), 4.21(m, 2H), 3.33(s, 2H), 2.96(dd, 1H), 1.09-1.97(m, 13H), 0.88(dd, 6H)

Example 174

N-(2,3-Dichlorobenzyl)-N-(cyclopentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.81-7.67(m, 9H), 6.05(bs, 1H), 5.31(dd, 2H), 5.11(d, 1H), 4.63(m, 3H), 4.15(m, 1H), 3.33(s, 2H), 2.96(dd, 1H), 1.26-2.05(m, 11H), 0.87(m, 6H)

Example 175

N-(2,3-Dichlorobenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 8.19(bs, 1H), 6.58-7.62(m, 12H), 5.22(m, 3H), 4.74(m, 2H), 4.36(m, 1H), 3.35(s, 2H), 3.09(dd, 1H), 1.26-1.54(m, 3H), 0.89(d, 6H)

Example 176

N-(2,3-Dichlorobenzyl)-N-[2-(dimethylamino)ethylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.87-7.66(m, 9H), 5.32(dd, 2H), 4.56-4.82(m, 3H), 4.29(m, 1H), 3.56(m, 1H), 3.32(d, 2H), 3.12(dd, 1H), 2.77(m, 1H), 2.52(m, 2H), 2.07(s, 6H), 1.24-1.61(m, 3H), 0.92(d, 6H)

Example 177

N-(2,3-Dichlorobenzyl)-N-[4-(dimethylamino)phenylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.81(bs, 1H), 6.57-7.59(m, 13H), 5.25(m, 3H), 4.77(m, 2H), 4.27(m, 1H), 3.33(s, 2H), 3.01(m, 7H), 1.27-1.59(m, 3H), 0.91(d, 6H)

Example 178

N-(2,3-Dichlorobenzyl)-N-[3-(dimethylamino)propylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 8.79(bs, 1H), 6.87-7.68(m, 9H), 5.36(m, 3H),

4.63(m, 2H), 4.28(m, 1H), 3.65(m, 2H), 3.32(m, 2H), 2.94(dd, 1H), 1.24-2.56(m, 15H), 0.89(d, 6H)

Example 179

N-(2,3-Dichlorobenzyl)-N-(3-ethoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.86-7.66(m, 9H), 5.33(dd, 2H), 4.88(m, 1H), 4.59(m, 2H), 4.23(m, 1H), 3.73(q, 2H), 3.11-3.55(m, 6H), 2.96(dd, 1H), 1.77(m, 2H), 1.15-1.57(m, 3H), 0.89(m, 9H)

Example 180

N-(2,3-Dichlorobenzyl)-N-(ethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.88-7.66(m, 9H), 6.39(bs, 1H), 5.31(dd, 2H), 5.06(d, 1H), 4.58(m, 2H), 4.14(m, 1H), 3.68(m, 2H), 3.31(s, 2H), 2.96(dd, 1H), 1.11-1.54(m, 6H), 0.88(m, 6H)

Example 181

N-(2,3-Dichlorobenzyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 8.21(bs, 1H), 6.79-7.61(m, 13H), 5.23(m, 3H), 4.71(m, 2H), 4.34(m, 1H), 3.34(s, 2H), 3.05(dd, 1H), 1.29-1.54(m, 3H), 0.88(d, 6H)

Example 182

N-(2,3-Dichlorobenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.84(bs, 1H), 6.81-7.59(m, 13H), 5.51(d, 1H), 5.24(s, 2H), 4.75(d, 1H), 4.58(m, 1H), 4.19(m, 1H), 3.34(s, 2H), 3.05(dd, 1H), 1.25-1.53(m, 3H), 0.88(m, 6H)

Example 183

N-(2,3-Dichlorobenzyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.54(bs, 1H), 6.76-7.61(m, 13H), 5.23-5.47(m, 3H), 4.74(m, 2H), 4.21(m, 1H), 3.32(s, 2H), 3.05(dd, 1H), 1.25-1.515(m, 3H), 0.87(m, 6H)

Example 184

N-(2,3-Dichlorobenzyl)-N-(4-hydroxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.93-7.66(m, 13H), 5.42(d, 2H), 5.02(dd, 2H), 4.33(m, 1H), 3.92(m, 1H), 3.46(dd, 1H), 3.31(d, 2H), 1.33-1.58(m, 3H), 0.87(m, 6H)

Example 185

N-(2,3-Dichlorobenzyl)-N-(4-isopropylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.19(bs, 1H), 6.82-7.59(m, 9H), 5.31(m, 3H), 4.75(m, 2H), 4.25(m, 1H), 3.34(s, 2H), 3.05(dd, 1H), 2.89(m, 1H), 1.03-1.56(m, 9H), 0.88(d, 6H)

Example 186

N-(2,3-Dichlorobenzyl)-N-(2-methoxyethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.89-7.66(m, 13H), 6.28(bs, 1H), 5.33(dd, 2H), 4.84(m, 2H), 4.39(d, 1H), 4.25(m, 1H), 3.01-3.86(m, 10H), 1.25-1.58(m, 3H), 0.89(d, 6H)

Example 187

N-(2,3-Dichlorobenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 8.21(d, 1H), 6.77-7.64(m, 13H), 5.17(s, 2H), 5.03(m, 2H), 4.73(d, 1H), 4.41(m, 1H), 3.57(s, 3H), 3.35(s, 2H), 3.12(dd, 1H), 1.25-1.61(m, 3H), 0.91(d, 6H)

Example 188

N-(2,3-Dichlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 8.21(bs, 1H), 6.81-7.61(m, 13H), 5.25(m, 3H), 4.74(m, 2H), 4.27(m, 1H), 3.78(s, 3H), 3.32(s, 2H), 3.05(dd, 1H), 1.25-1.55(m, 3H), 0.88(d, 6H)

Example 189

N-(2,3-Dichlorobenzyl)-N-(3-methoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.83-7.66(m, 9H), 5.33(dd, 2H), 4.93(m, 1H), 4.59(dd, 2H), 4.24(m, 1H), 3.65(m, 2H), 2.91-3.47(m, 8H), 1.19-1.78(m, 5H), 0.87(d, 6H)

Example 190

N-(2,3-Dichlorobenzyl)-N-(2-methoxypyridin-5-ylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.81(bs, 1H), 6.67-7.94(m, 12H), 5.31(m, 3H), 4.69(m, 2H), 4.23(m, 1H), 3.87(s, 3H), 3.32(s, 2H), 3.07(dd, 1H), 1.25-1.55(m, 3H), 0.87(d, 6H)

Example 191

N-(2,3-Dichlorobenzyl)-N-(methylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.93-7.66(m, 9H), 6.71(bs, 1H), 5.31(dd, 2H), 5.05(d, 1H), 4.58(m, 2H), 4.14(m, 1H), 3.31(s, 3H), 3.08(d, 2H), 2.93(dd, 1H), 1.25-1.58(m, 3H), 0.87(m, 6H)

Example 192

N-(2,3-Dichlorobenzyl)-N-(4-methylthiophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.48(bs, 1H), 6.78-7.59(m, 13H), 5.29(m, 3H), 4.71(m, 2H), 4.22(m, 1H), 3.33(s, 2H), 3.04(dd, 1H), 2.45(s, 3H), 1.25-1.55(m, 3H), 0.87(m, 6H)

Example 193

N-(2,3-Dichlorobenzyl)-N-(2-naphthylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.72(bs, 1H), 6.78-7.89(m, 16H), 5.31(m, 3H),

4.81(m, 2H), 4.29(m, 1H), 3.36(s, 2H), 3.07(dd, 1H), 1.27-1.54(m, 3H), 0.89(d, 6H)

Example 194

N-(2,3-Dichlorobenzyl)-N-(4-nitrophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 9.46(bs, 1H), 6.69-8.16(m, 13H), 5.73(d, 1H), 5.24(s, 2H), 4.74(d, 1H), 4.32(m, 1H), 4.16(m, 1H), 3.38(s, 2H), 3.06(dd, 1H), 1.25-1.55(m, 3H), 0.88(d, 6H)

Example 195

N-(2,3-Dichlorobenzyl)-N-(n-pentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.91-7.66(m, 9H), 6.21(bs, 1H), 5.33(dd, 2H), 5.04(d, 1H), 4.62(m, 2H), 4.18(m, 1H), 2.95-3.73(m, 5H), 0.74-1.71(m, 18H)

Example 196

N-(2,3-Dichlorobenzyl)-N-(phenethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.74-7.64(m, 14H), 5.93(bs, 1H), 5.29(dd, 2H), 4.69(m, 2H), 4.45(d, 1H), 4.17(m, 1H), 3.86(m, 2H), 3.29(s, 2H), 2.79-3.02(m, 3H), 1.23-1.56(m, 3H), 0.88(d, 6H)

Example 197

N-(2,3-Dichlorobenzyl)-N-(phenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.38(bs, 1H), 6.79-7.57(m, 14H), 5.29(m, 3H), 4.75(m, 2H), 4.26(m, 1H), 3.33(s, 2H), 3.05(dd, 1H), 1.25-1.55(m, 3H), 0.87(m, 6H)

Example 198

N-(2,3-Dichlorobenzyl)-N-(n-propylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.89-7.66(m, 9H), 6.35(bs, 1H), 5.31(dd, 2H), 5.05(d, 1H), 4.63(m, 2H), 4.16(m, 1H), 3.66(m, 1H), 3.49(m, 1H), 3.32(s, 2H), 2.93(dd, 1H), 1.26-1.61(m, 5H), 0.87(m, 9H)

Example 199

N-(2,3-Dichlorobenzyl)-N-(3-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.19(bs, 1H), 6.76-7.57(m, 13H), 5.29(m, 3H), 4.71(m, 2H), 4.27(m, 1H), 3.34(s, 2H), 3.05(dd, 1H), 2.31(m, 3H), 1.25-1.55(m, 3H), 0.91(d, 6H)

Example 200

N-(2,3-Dichlorobenzyl)-N-(2-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.78(bs, 1H), 6.78-7.61(m, 13H), 5.29(m, 3H), 4.81(m, 2H), 4.29(m, 1H), 3.33(s, 2H), 3.09(dd, 1H), 2.09(s, 3H), 1.25-1.53(m, 3H), 0.91(d, 6H)

Example 201

N-(2,3-Dichlorobenzyl)-N-(4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.21(bs, 1H), 6.81-7.61(m, 13H), 5.31(m, 3H), 4.75(m, 2H), 4.26(m, 1H), 3.34(s, 2H), 3.06(dd, 1H), 2.34(s, 3H), 1.26-1.56(m, 3H), 0.89(d, 6H)

Example 202

N-(2,3-Dichlorobenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 9.16(bs, 1H), 6.71-7.78(m, 13H), 5.64(d, 1H), 5.25(s, 2H), 4.78(d, 1H), 4.46(m, 1H), 4.16(m, 1H), 3.34(s, 2H), 3.06(dd, 1H), 1.26-1.54(m, 3H), 0.89(m, 6H)

Example 203

N-(2,3-Dichlorobenzyl)-N-(2,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.81-7.61(m, 12H), 5.25(m, 3H), 4.79(m, 2H), 4.31(m, 1H), 3.34(s, 2H), 3.08(dd, 1H), 2.31(s, 3H), 2.05(s, 3H), 1.26-1.54(m, 3H), 0.89(d, 6H)

Example 204

N-(2,3-Dichlorobenzyl)-N-(3,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.01(bs, 1H), 6.79-7.61(m, 12H), 5.29(m, 3H), 4.76(m, 2H), 4.28(m, 1H), 3.36(s, 2H), 3.06(dd, 1H), 2.23(m, 6H), 1.27-1.53(m, 3H), 0.91(d, 6H)

Example 205

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

<Step 1>

N-(2,3-Dichlorobenzyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

Using the same method as described in Preparative Example 3, 2-(t-butoxycarbonyl)amino-2-methylpropionic acid was converted to 2-(t-butoxycarbonyl)amino-2-methylpropion aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid HCl with 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid HCl to give the title compound.

¹H-NMR(CDCl₃) : δ 7.61(d, 2H), 7.53(s, 1H), 7.22(d, 2H), 7.16(d, 2H), 7.01(s, 1H), 6.43(bs, 1H), 5.26(s, 2H), 3.82(s, 2H), 3.35(s, 2H), 2.58(s, 2H), 1.23(s, 6H)

<Step 2>

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

To a solution of N-(2,3-dichlorobenzyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine in methylene chloride (0.02M, 1ml, 0.02mmol) was added allylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 1hr at room temperature. The mixture was purified by silica gel column

chromatography(eluent: methylene chloride/methanol=9/1, v/v) to give the title compound as a white solid.

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.20(bs, 1H), 7.65(d, 2H), 7.45(m, 2H), 7.20(m, 3H), 7.00(s, 1H), 6.95(d, 1H), 6.40(bs, 1H), 5.80(m, 1H), 5.35(s, 2H), 5.10(m, 2H), 4.98(m, 2H), 4.24(t, 2H), 3.98(s, 2H), 3.25(s, 2H), 1.40(s, 6H)

Examples 206-251

N-(2,3-Dichlorobenzyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 205 to give the title compounds.

Example 206

N-(2,3-Dichlorobenzyl)-N-(benzylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.45(m, 2H), 7.25(m, 4H), 7.15(m, 4H), 6.95(m, 2H), 5.30(s, 2H), 5.00(s, 2H), 4.80(d, 2H), 4.00(s, 2H), 1.40(s, 6H)

Example 207

N-(2,3-Dichlorobenzyl)-N-(2-biphenylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 3H), 7.38(m, 4H), 7.30(s, 7H), 7.10(d, 3H), 6.95(s, 1H), 6.70(d, 1H), 5.27(s, 2H), 4.82(s, 2H), 3.95(s, 2H), 3.20(s, 2H), 1.40(s, 6H)

Example 208

N-(2,3-Dichlorobenzyl)-N-(2-bromophenylthiocarbamoyl)-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.60(m, 4H), 7.45(m, 2H), 7.30(m, 3H), 7.15(m, 4H), 6.95(s, 1H), 5.30(s, 2H), 5.10(s, 2H), 4.10(s, 2H), 3.20(s, 2H), 1.50(s, 6H)

Example 209

N-(2,3-Dichlorobenzyl)-N-(3-bromophenylthiocarbamoyl)-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.60(d, 2H), 7.45(m, 4H), 7.25(m, 3H), 7.10(d, 3H), 6.95(s, 1H), 5.30(s, 2H), 5.25(s, 2H), 3.98(s, 2H), 3.27(s, 2H), 1.45(s, 6H)

Example 210

N-(2,3-Dichlorobenzyl)-N-(4-bromophenylthiocarbamoyl)-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.60(d, 2H), 7.43(m, 4H), 7.22(m, 4H), 7.08(d, 3H), 6.95(s, 1H), 5.22(s, 4H), 3.98(s, 2H), 3.25(s, 2H), 1.44(s, 6H)

Example 211

N-(2,3-Dichlorobenzyl)-N-(n-butylthiocarbamoyl)-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.65(d, 2H), 7.45(m, 2H), 7.20(m, 3H), 7.00(s, 1H), 6.90(d, 1H), 6.06bs, 1H), 5.37(s, 2H), 4.98(s, 2H), 3.98(s, 2H),

3.58(q, 2H), 3.27(s, 2H), 1.50(m, 2H), 1.40(s, 6H), 1.20(m, 2H), 0.86(t, 3H)

Example 212

N-(2,3-Dichlorobenzyl)-N-(isobutylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.45(m, 2H), 7.20(m, 3H), 7.00(s, 1H), 6.95(d, 1H), 6.00(bs, 1H), 5.38(s, 2H), 4.90(s, 2H), 4.00(s, 2H), 3.40(t, 2H), 3.25(s, 2H), 1.80(m, 1H), 1.40(s, 6H), 0.80(d, 6H)

Example 213

N-(2,3-Dichlorobenzyl)-N-(t-butylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.48(m, 2H), 7.20(m, 3H), 7.00(s, 1H), 6.95(d, 1H), 5.40(s, 2H), 4.80(s, 2H), 4.02(s, 2H), 3.25(s, 2H), 1.45(s, 6H), 1.40(s, 9H)

Example 214

N-(2,3-Dichlorobenzyl)-N-(2-chlorophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 3H), 7.20-7.50(m, 7H), 7.12(d, 3H), 6.97(s, 1H), 5.35(s, 2H), 5.15(s, 2H), 4.10(s, 2H), 3.25(s, 2H), 1.48(s, 6H)

Example 215

N-(2,3-Dichlorobenzyl)-N-(3-chlorophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.43(d, 2H), 7.28(m, 5H), 7.10(d, 3H), 6.95(s, 1H), 5.30(s, 2H), 5.27(s, 2H), 3.98(s, 2H), 3.27(s, 2H), 1.47(s, 6H)

Example 216

N-(2,3-Dichlorobenzyl)-N-(4-chlorophenylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.45(s, 2H), 7.28(s, 5H), 7.08(d, 3H), 6.95(s, 1H), 5.25(s, 2H), 5.20(s, 2H), 3.98(s, 2H), 3.25(s, 2H), 1.43(s, 6H)

Example 217

N-(2,3-Dichlorobenzyl)-N-(3-chloro-4-methylphenylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.45(m, 2H), 7.23(m, 2H), 7.20(s, 2H), 7.10(d, 2H), 6.95(s, 1H), 6.40(bs, 1H), 5.80(m, 1H), 5.35(s, 2H), 5.22(s, 2H), 3.98(s, 2H), 3.25(s, 2H), 2.39(s, 3H), 1.45(s, 6H)

Example 218

N-(2,3-Dichlorobenzyl)-N-(cyclohexylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.53(s, 1H), 7.45(d, 1H), 7.20(t, 3H), 7.00(s, 1H), 6.95(d, 1H), 5.70(bs, 1H), 5.40(s, 2H), 4.90(s, 2H), 4.20(m, 1H), 3.98(s, 2H), 3.25(s, 2H), 1.90(m, 2H), 1.60(m, 2H), 1.40(s, 6H), 1.15(m, 2H), 1.10(m, 4H)

Example 219

N-(2,3-Dichlorobenzyl)-N-(cyclopentylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.52(s, 1H), 7.45(d, 1H), 7.20(t, 3H), 7.00(s, 1H), 6.95(d, 1H), 5.90(bs, 1H), 5.38(s, 2H), 4.92(s, 2H), 4.62(q, 1H), 3.98(s, 2H), 3.25(s, 2H), 2.00(m, 4H), 1.53(m, 4H), 1.40(s, 6H)

Example 220

N-(2,3-Dichlorobenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.45(t, 2H), 7.40(m, 2H), 7.24(m, 2H), 7.10(d, 3H), 6.95(s, 1H), 5.30(s, 2H), 5.15(s, 2H), 4.06(s, 2H), 3.22(s, 2H), 1.45(s, 6H)

Example 221

N-(2,3-Dichlorobenzyl)-N-[2-(dimethylamino)ethylthiocarbamoyl]-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.51(s, 1H), 7.45(d, 1H), 7.20(d, 3H), 7.00(s, 1H), 6.90(d, 1H), 5.40(s, 2H), 4.80(s, 2H), 4.10(s, 2H), 3.50(s, 2H), 3.26(s, 2H), 2.40(t, 2H), 2.00(s, 6H), 1.45(s, 6H)

Example 222

N-(2,3-Dichlorobenzyl)-N-[4-(dimethylamino)phenylthiocarbamoyl]-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.58(d, 2H), 7.45(m, 2H), 7.27(m, 1H), 7.10(m, 2H), 7.05(m, 3H), 6.65(d, 2H), 5.35(s, 2H), 5.10(s, 2H), 4.04(s, 2H), 3.25(s, 2H), 2.95(s, 6H), 1.45(s, 6H)

Example 223

N-(2,3-Dichlorobenzyl)-N-(ethoxycarbonylmethylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.47(s, 2H), 7.20(t, 3H), 6.98(m, 2H), 5.35(s, 2H), 5.00(s, 2H), 4.34(d, 2H), 4.20(q, 2H), 3.98(s, 2H), 3.25(s, 2H), 1.44(s, 6H), 1.25(t, 3H)

Example 224

N-(2,3-Dichlorobenzyl)-N-(3-ethoxypropylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.45(m, 2H), 7.20(t, 3H), 7.00(s, 1H), 6.95(s, 1H), 6.80(d, 1H), 5.40(s, 2H), 4.80(s, 2H), 3.98(s, 2H), 3.73(q, 2H), 3.42(t, 2H), 3.25(m, 4H), 1.78(p, 2H), 1.42(s, 6H), 1.00(t, 3H)

Example 225

N-(2,3-Dichlorobenzyl)-N-(ethylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.45(m, 2H), 7.20(t, 3H), 7.00(s, 1H), 6.95(d, 1H), 6.20(bs, 1H), 5.38(s, 2H), 4.98(s, 2H), 3.98(s, 2H), 3.62(p, 2H), 3.25(s, 2H), 1.40(s, 6H), 1.14(t, 3H)

Example 226

N-(2,3-Dichlorobenzyl)-N-(2-fluorophenylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.40(m, 3H), 7.27(m, 2H), 7.20(m,

5H), 6.95(s, 1H), 5.35(s, 2H), 5.18(s, 2H), 4.04(s, 2H), 3.25(s, 2H), 1.45(s, 6H)

Example 227

N-(2,3-Dichlorobenzyl)-N-(3-fluorophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.60(d, 2H), 7.45(m, 2H), 7.04-7.30(m, 7H), 7.20(m, 3H), 6.95(m, 2H), 5.32(s, 2H), 5.28(s, 2H), 3.98(s, 2H), 3.30(s, 2H), 1.46(s, 6H)

Example 228

N-(2,3-Dichlorobenzyl)-N-(4-fluorophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.60(d, 2H), 7.45(m, 2H), 7.22(m, 3H), 7.10(d, 3H), 7.00(s, 1H), 6.95(s, 1H), 5.30(s, 2H), 5.20(s, 2H), 4.00(s, 2H), 3.25(s, 2H), 1.40(s, 6H)

Example 229

N-(2,3-Dichlorobenzyl)-N-(4-hydroxyphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.58(d, 2H), 7.40(d, 2H), 7.25(m, 2H), 7.10(d, 3H), 6.95(s, 2H), 6.75(d, 2H), 5.30(s, 2H), 5.05(s, 2H), 4.00(bs, 2H), 3.25(s, 2H), 1.45(s, 6H)

Example 230

N-(2,3-Dichlorobenzyl)-N-(4-isopropylphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.45(s, 2H), 7.25(s, 2H), 7.20(s, 3H), 7.10(d, 3H), 6.95(s, 1H), 5.30(s, 2H), 5.10(s, 2H), 4.05(s, 2H), 3.25(s, 2H), 2.90(q, 1H), 1.45(s, 6H), 1.12(d, 6H)

Example 231

N-(2,3-Dichlorobenzyl)-N-(2-methoxyethylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-}5\text{-yl]acetyl}\}$ amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.45(m, 2H), 7.20(t, 3H), 7.00(s, 1H), 6.95(d, 1H), 6.25(bs, 1H), 5.40(s, 2H), 4.90(s, 2H), 4.04(s, 2H), 3.75(q, 2H), 3.40(t, 2H), 3.25(s, 2H), 3.13(s, 3H), 1.40(s, 6H)

Example 232

N-(2,3-Dichlorobenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-}5\text{-yl]acetyl}\}$ amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.10(d, 1H), 7.65(s, 1H), 7.60(d, 2H), 7.48(s, 2H), 7.25(t, 1H), 7.12(d, 3H), 7.00(t, 3H), 6.90(d, 1H), 5.38(s, 2H), 5.00(s, 2H), 4.20(s, 2H), 3.60(s, 3H), 3.25(s, 2H), 1.45(s, 6H)

Example 233

N-(2,3-Dichlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-}5\text{-yl]acetyl}\}$ amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.45(s, 2H), 7.27(m, 1H), 7.10(m, 5H), 7.00(s, 1H), 6.85(d, 2H), 5.30(s, 2H), 5.10(s, 2H), 4.00(s, 2H), 3.80(s, 3H), 3.25(s, 2H), 1.42(s, 6H)

Example 234

N-(2,3-Dichlorobenzyl)-N-(3-methoxypropylthiocarbamoyl)-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.65(d, 2H), 7.45(m, 2H), 7.20(t, 3H), 7.00(s, 2H), 6.90(d, 1H), 5.40(s, 2H), 4.80(s, 2H), 4.00(s, 2H), 3.68(q, 2H), 3.40(t, 2H), 3.25(s, 2H), 3.00(s, 3H), 1.76(p, 2H), 1.40(s, 6H)

Example 235

N-(2,3-Dichlorobenzyl)-N-(2-methoxypyridin-5-ylthiocarbamoyl)-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.90(s, 1H), 7.60(d, 3H), 7.40(m, 2H), 7.25(t, 1H), 7.10(d, 3H), 6.90(s, 1H), 6.80(d, 1H), 5.30(s, 2H), 5.20(s, 2H), 4.00(s, 2H), 3.90(s, 3H), 3.25(s, 2H), 1.45(s, 6H)

Example 236

N-(2,3-Dichlorobenzyl)-N-(methylthiocarbamoyl)-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.65(d, 2H), 7.45(s, 2H), 7.20(t, 3H), 7.00(s, 1H), 6.90(d, 1H), 6.55(bs, 1H), 5.40(s, 2H), 4.95(s, 2H), 3.98(s, 2H), 3.25(s, 2H), 3.08(d, 3H), 1.40(s, 6H)

Example 237

N-(2,3-Dichlorobenzyl)-N-(4-methylthiophenylthiocarbamoyl)-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.60(d, 2H), 7.45(s, 2H), 7.28(s, 1H), 7.20(s, 4H), 7.10(d, 2H), 6.95(s, 1H), 5.25(s, 2H), 5.20(s, 2H), 4.00(s, 2H), 3.25(s, 2H), 2.45(s, 3H), 1.40(s, 6H)

Example 238

N-(2,3-Dichlorobenzyl)-N-(2-naphthylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60-7.85(m, 4H), 7.45(m, 7H), 7.30(t, 2H), 7.15(d, 1H), 6.95(d, 3H), 5.28(s, 2H), 5.20(s, 2H), 4.00(s, 2H), 3.25(s, 2H), 1.45(s, 6H)

Example 239

N-(2,3-Dichlorobenzyl)-N-(4-nitrophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.18(d, 2H), 7.73(d, 2H), 7.47(t, 3H), 7.42(d, 1H), 7.25(m, 1H), 7.10(d, 3H), 6.00(s, 1H), 5.37(s, 2H), 5.25(s, 2H), 3.92(s, 2H), 3.35(s, 2H), 1.42(s, 6H)

Example 240

N-(2,3-Dichlorobenzyl)-N-(n-pentylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.45(m, 2H), 7.20(t, 3H), 7.00(s, 1H), 6.95(d, 1H), 5.95(bs, 1H), 5.40(s, 2H), 5.10(m, 2H), 4.90(s, 2H), 3.42(m, 2H), 3.25(s, 2H), 1.60(p, 2H), 1.40(s, 6H), 1.10(m, 2H), 0.80(m, 5H)

Example 241

N-(2,3-Dichlorobenzyl)-N-(phenethylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.45(m, 2H), 7.18(d, 6H), 7.00(s, 1H),

6.95(m, 2H), 6.72(d, 1H), 5.80(bs, 1H), 5.40(s, 2H), 4.70(s, 2H), 3.98(s, 2H), 3.82(q, 2H), 3.25(s, 2H), 2.80(t, 2H), 1.40(s, 6H)

Example 242

N-(2,3-Dichlorobenzyl)-N-(phenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.55(d, 2H), 7.45(s, 2H), 7.30(m, 5H), 7.10(t, 3H), 6.95(s, 1H), 5.30(s, 2H), 5.20(s, 2H), 4.00(s, 2H), 3.25(s, 2H), 1.44(s, 6H)

Example 243

N-(2,3-Dichlorobenzyl)-N-(n-propylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.65(d, 2H), 7.45(m, 2H), 7.20(t, 3H), 7.00(s, 1H), 6.95(d, 1H), 6.10(bs, 1H), 5.40(s, 2H), 4.95(s, 2H), 4.00(s, 2H), 3.55(q, 2H), 3.25(s, 2H), 1.54(q, 2H), 1.40(s, 6H), 0.80(t, 3H)

Example 244

N-(2,3-Dichlorobenzyl)-N-(3-methylphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.60(d, 2H), 7.45(d, 2H), 7.25(m, 3H), 7.08(d, 5H), 6.97(s, 1H), 5.28(s, 2H), 5.17(s, 2H), 4.02(s, 2H), 3.25(s, 2H), 2.38(s, 3H), 1.40(s, 6H)

Example 245

N-(2,3-Dichlorobenzyl)-N-(2-methylphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.45(m, 2H), 7.25(m, 4H), 7.10(t, 4H), 6.95(s, 1H), 5.30(s, 2H), 5.10(s, 2H), 4.10(s, 2H), 3.25(s, 2H), 2.10(s, 3H), 1.40(s, 6H)

Example 246

N-(2,3-Dichlorobenzyl)-N-(4-methylphenylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-}5\text{-yl]acetyl}\}$ amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.57(d, 2H), 7.45(s, 2H), 7.26(t, 2H), 7.12(m, 6H), 6.95(s, 1H), 5.30(s, 2H), 5.17(s, 2H), 4.00(s, 2H), 3.25(s, 2H), 2.38(s, 3H), 1.40(s, 6H)

Example 247

N-(2,3-Dichlorobenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-}5\text{-yl]acetyl}\}$ amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.78(bs, 1H), 7.60(d, 3H), 7.45(m, 4H), 7.26(t, 1H), 7.10(t, 4H), 6.95(s, 1H), 5.30(s, 4H), 3.95(s, 2H), 3.25(s, 2H), 1.45(s, 6H)

Example 248

N-(2,3-Dichlorobenzyl)-N-(2,4-dimethylphenylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-}5\text{-yl]acetyl}\}$ amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.45(m, 2H), 7.24(d, 1H), 7.12(d, 3H), 7.00(bs, 2H), 6.95(d, 2H), 5.30(s, 2H), 5.10(s, 2H), 4.10(s, 2H), 3.25(s, 2H), 2.32(s, 3H), 2.05(s, 3H), 1.45(s, 6H)

Example 249

N-(2,3-Dichlorobenzyl)-N-(3,4-dimethylphenylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.57(d, 2H), 7.45(s, 2H), 7.25(m, 1H), 7.10(d, 4H), 6.95(s, 3H), 5.30(s, 2H), 5.10(s, 2H), 4.23(s, 2H), 3.25(s, 2H), 2.24(s, 6H), 1.40(s, 6H)

Example 250

N-(2,3-Dichlorobenzyl)-N-(3-dimethylaminopropylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 9.20(bs, 1H), 7.56(d, 2H), 7.42-7.48(m, 2H), 7.16-7.23(m, 3H), 7.00(s, 3H), 6.90(d, 2H), 5.40(s, 2H), 4.80(s, 2H), 3.90(bs, 2H), 3.71(m, 2H), 2.40(t, 2H), 1.95(s, 6H), 1.45(s, 6H)

Example 251

N-(2,3-Dichlorobenzyl)-N-(ethoxycarbonylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.50-7.75(m, 5H), 7.43-7.46(m, 1H), 7.18-7.25(m, 2H), 7.00(s, 1H), 5.28-5.33(m, 4H), 5.15(bs, 2H), 4.19-4.25(m, 4H), 3.50(s, 2H), 1.42(s, 6H), 1.25(t, 3H)

Example 252

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2(S)- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

<Step 1>

N-(2,3-Dichlorobenzyl)-2(S)- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

The title compound was prepared by using the same procedure as Preparative Example 4, but replacing N-t-butoxycarbonyl-L-isoleucine aldehyde and 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid HCl with L-2-(t-butoxycarbonyl)aminobutyraldehyde and 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid, respectively.

$^1\text{H-NMR}(\text{CDCl}_3)$ δ 7.61(d, 2H), 7.52(s, 1H), 7.38(dd, 2H), 7.11-7.21(m, 4H), 7.01(s, 1H), 6.08(d, 1H), 5.26(s, 2H), 3.83-3.92(m, 3H), 3.35(s, 2H), 2.62(d, 2H), 1.33-1.51(m, 2H), 0.84(t, 3H)

<Step 2>

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

To a solution of N-(2,3-dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine in methylene chloride (0.02M, 1ml, 0.02mmol) was added allylthiocyanate (0.1M in CH_2Cl_2 , 0.2ml, 0.02mmol). The reaction mixture was agitated for 1hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: methylene chloride/methanol=9/1, v/v) to give the title compound as a white solid.

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.50(s, 1H), 7.41(d, 1H), 7.18(m, 3H), 7.05(d, 1H), 7.00(m, 2H), 6.42(bs, 1H), 5.85(m, 1H), 5.33(q, 2H), 5.07(m, 3H), 4.75(m, 1H), 4.68(d, 1H), 4.30(q, 2H), 4.01(m, 1H), 3.32(s, 2H), 3.00(dd, 1H), 1.55(m, 2H), 0.90(t, 3H)

Examples 253-297

N-(2,3-Dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 252 to give the title compounds.

Example 253

N-(2,3-Dichlorobenzyl)-N-(benzylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.42(s, 2H), 7.40(s, 1H), 7.18(m, 8H), 6.95(m, 2H), 6.80(bs, 1H), 5.23(d, 2H), 5.10(d, 1H), 4.85(m, 2H), 4.80(m, 1H), 4.60(d, 1H), 4.05(m, 1H), 3.27(s, 2H), 1.57(m, 2H), 0.90(t, 3H)

Example 254

N-(2,3-Dichlorobenzyl)-N-(2-biphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.68(d, 1H), 7.58(d, 2H), 7.41(1, 1H), 7.30(m, 8H), 7.12(d, 2H), 7.01(s, 1H), 6.98(s, 2H), 6.69(d, 1H), 5.21(s, 2H), 5.12(bs, 1H), 4.51(d, 2H), 3.90(bs, 1H), 3.32(s, 2H), 2.95(dd, 1H), 1.60(m, 1H), 1.40(m, 1H), 0.85(t, 3H)

Example 255

N-(2,3-Dichlorobenzyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$ δ : 8.00(bs, 1H), 7.65(d, 1H), 7.58(d, 3H), 7.44(s, 2H), 7.30(m, 2H), 7.18(m, 4H), 6.98(m, 2H), 5.33(m, 1H), 5.24(s, 2H), 4.85(m, 1H), 4.78(d, 1H), 4.20(m, 1H), 3.39(s, 2H), 3.12(dd, 1H),

1.60(m, 2H), 0.90(t, 3H)

Example 256

N-(2,3-Dichlorobenzyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR (CDCl₃) : δ : 9.00(bs, 1H), 7.60(d, 2H), 7.50(m, 1H), 7.41(m, 3H), 7.30(m, 1H), 7.20(d, 2H), 7.10(m, 3H), 6.96(s, 2H), 5.63(d, 1H), 5.23(s, 2H), 4.68(d, 1H), 4.52(m, 1H), 4.01(m, 1H), 3.38(s, 2H), 3.05(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 257

N-(2,3-Dichlorobenzyl)-N-(4-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR (CDCl₃) : δ 8.70(bs, 1H), 7.60(d, 2H), 7.41(d, 4H), 7.24(m, 3H), 7.10(t, 3H), 7.00(s, 1H), 6.85(d, 1H), 5.55(d, 1H), 5.23(s, 2H), 4.68(d, 1H), 4.58(m, 1H), 4.01(m, 1H), 3.36(s, 2H), 3.05(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 258

N-(2,3-Dichlorobenzyl)-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.65(d, 2H), 7.50(s, 1H), 7.41(d, 1H), 7.18(m, 4H), 7.00(s, 1H), 6.95(s, 1H), 6.22(bs, 1H), 5.33(q, 2H), 5.07(d, 1H), 4.75(m, 1H), 4.58(d, 1H), 4.01(m, 1H), 3.60(m, 2H), 3.32(s, 2H), 3.00(dd, 1H), 1.55(m, 4H), 1.21(m, 2H), 0.89(q, 6H)

Example 259

N-(2,3-Dichlorobenzyl)-N-(isobutylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.50(s, 1H), 7.41(d, 1H), 7.18(m, 4H), 6.95(m, 2H), 6.20(bs, 1H), 5.33(q, 2H), 5.00(d, 1H), 4.80(m, 1H), 4.58(d, 1H), 4.01(m, 1H), 3.52(t, 1H), 3.32(s, 3H), 3.00(dd, 1H), 1.90(m, 1H), 1.58(m, 2H), 0.90(t, 3H), 0.80(t, 6H)

Example 260

N-(2,3-Dichlorobenzyl)-N-(t-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.52(s, 1H), 7.41(t, 2H), 7.18(m, 3H), 7.05(s, 1H), 6.90(d, 2H), 5.38(q, 2H), 5.07(m, 1H), 4.65(q, 2H), 4.01(m, 1H), 3.32(s, 2H), 3.00(dd, 1H), 1.55(m, 2H), 1.40(s, 9H), 0.90(t, 6H)

Example 261

N-(2,3-Dichlorobenzyl)-N-(2-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.00(bs, 1H), 7.60(m, 3H), 7.40(m, 3H), 7.20(m, 6H), 6.95(s, 2H), 5.33(s, 1H), 5.20(s, 2H), 4.85(m, 1H), 4.75(d, 1H), 4.20(m, 1H), 3.36(s, 2H), 3.12(dd, 1H), 1.58(m, 2H), 0.90(t, 3H)

Example 262

N-(2,3-Dichlorobenzyl)-N-(3-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.95(bs, 1H), 7.60(d, 2H), 7.40(m, 4H), 7.25(m, 3H), 7.15(m, 3H), 6.95(m, 2H), 5.60(d, 1H), 5.25(s, 2H), 4.68(d, 1H),

4.50(m, 1H), 4.01(m, 1H), 3.39(s, 2H), 3.05(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 263

N-(2,3-Dichlorobenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR (CDCl₃) : δ 8.70(bs, 1H), 7.60(d, 2H), 7.45(m, 2H), 7.30(s, 4H), 7.10(m, 3H), 7.95(m, 1H), 6.85(d, 1H), 5.55(d, 1H), 5.23(s, 2H), 4.70(d, 1H), 4.55(m, 1H), 4.01(m, 1H), 3.37(s, 2H), 3.05(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 264

N-(2,3-Dichlorobenzyl)-N-(3-chloro-4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 8.80(bs, 1H), 7.60(d, 2H), 7.45(d, 2H), 7.30(d, 2H), 7.25(s, 2H), 7.10(d, 3H), 6.95(s, 2H), 5.55(d, 1H), 5.25(s, 2H), 4.68(d, 1H), 4.59(m, 1H), 4.01(m, 1H), 3.38(s, 2H), 3.04(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.92(t, 3H)

Example 265

N-(2,3-Dichlorobenzyl)-N-(cyclohexylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.65(d, 2H), 7.53(s, 1H), 7.41(d, 1H), 7.18(m, 4H), 7.02(d, 1H), 6.92(d, 2H), 5.85(bs, 1H), 5.33(q, 2H), 5.05(m, 1H), 4.80(m, 1H), 4.60(d, 1H), 4.30(m, 1H), 4.00(m, 1H), 3.36(s, 2H), 3.00(dd, 1H), 2.00(m, 2H), 1.20-1.70(m, 8H), 1.10(m, 2H), 0.90(t, 3H)

Example 266

N-(2,3-Dichlorobenzyl)-N-(cyclopentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.55(s, 1H), 7.41(d, 1H), 7.18(d, 3H), 7.08(d, 1H), 7.05(m, 1H), 6.95(d, 1H), 6.05(s, 1H), 5.35(q, 2H), 5.07(d, 1H), 4.70(h, 1H), 4.58(d, 1H), 4.00(m, 1H), 3.36(s, 2H), 3.00(dd, 1H), 2.00(m, 2H), 1.23-1.65(m, 8H), 0.90(t, 3H)

Example 267

N-(2,3-Dichlorobenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.20(bs, 1H), 7.60(t, 2H), 7.45(m, 3H), 7.25(d, 2H), 7.10(d, 3H), 6.95(s, 1H), 6.90(d, 1H), 5.35(m, 1H), 5.25(s, 2H), 4.75(d, 2H), 4.19(m, 1H), 3.38(s, 2H), 3.12(dd, 1H), 1.55(m, 2H), 0.90(t, 3H)

Example 268

N-(2,3-Dichlorobenzyl)-N-[(2-dimethylamino)ethylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.50(s, 1H), 7.35(m, 2H), 7.20(d, 2H), 7.05(s, 1H), 6.90(d, 2H), 5.38(q, 2H), 4.90(m, 2H), 4.60(d, 1H), 4.10(m, 1H), 3.55(m, 2H), 3.35(s, 2H), 3.12(dd, 1H), 2.48(m, 2H), 1.80(s, 6H), 1.55(m, 2H), 0.90(t, 3H)

Example 269

N-(2,3-Dichlorobenzyl)-N-[(4-dimethylamino)phenylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.90(bs, 1H), 7.60(d, 2H), 7.45(m, 2H), 7.20(m, 1H), 7.10(m, 4H), 7.00(d, 2H), 6.62(d, 2H), 5.28(s, 2H), 5.20(d, 1H), 4.90(m, 1H), 4.70(d, 1H), 4.10(m, 1H), 3.38(s, 2H), 3.08(dd, 1H), 2.95(s, 6H), 1.55(m, 2H), 0.90(t, 3H)

Example 270

N-(2,3-Dichlorobenzyl)-N-[(3-dimethylamino)propylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.95(bs, 1H), 7.65(d, 3H), 7.50(s, 1H), 7.41(d, 1H), 7.18(d, 3H), 7.03(s, 1H), 6.90(d, 1H), 6.42(bs, 1H), 5.40(q, 2H), 5.04(m, 1H), 4.58(s, 2H), 4.03(m, 1H), 3.64(m, 2H), 3.32(q, 2H), 2.96(dd, 1H), 2.37(m, 2H), 1.78(s, 8), 1.55(m, 2H), 0.90(t, 3H)

Example 271

N-(2,3-Dichlorobenzyl)-N-(ethoxycarbonylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.43(m, 2H), 7.18(m, 3H), 7.00(m, 4H), 5.32(s, 2H), 5.10(d, 1H), 4.75(m, 1H), 4.65(d, 1H), 4.33(m, 2H), 4.15(q, 3H), 3.38(s, 2H), 3.02(dd, 1H), 1.55(m, 2H), 1.25(t, 3H), 0.90(t, 3H)

Example 272

N-(2,3-Dichlorobenzyl)-N-(3-ethoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.52(s, 1H), 7.41(d, 2H), 7.18(m, 3H), 7.03(s, 1H), 86(d, 2H), 5.36(q, 2H), 5.00(t, 1H), 4.60(q, 2H), 4.05(m,

1H), 3.72(q, 2H), 3.42(h, 2H), 3.32(s, 2H), 3.20(t, 2H), 2.96(dd, 1H), 1.76(q, 2H), 1.50(m, 2H), 0.90(m, 6H)

Example 273

N-(2,3-Dichlorobenzyl)-N-(ethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.65(d, 2H), 7.50(s, 1H), 7.41(d, 1H), 7.18(m, 4H), 6.96(m, 2H), 6.40(bs, 1H), 5.35(q, 2H), 5.10(d, 1H), 4.70(m, 1H), 4.55(d, 1H), 4.00(m, 1H), 3.62(h, 2H), 3.35(s, 2H), 2.98(dd, 1H), 1.55(m, 2H), 1.15(t, 3H), 0.90(t, 3H)

Example 274

N-(2,3-Dichlorobenzyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 8.18(bs, 1H), 7.60(d, 2H), 7.40(m, 3H), 7.22(m, 2H), 7.10(m, 3H), 7.00(s, 1H), 5.38(m, 1H), 5.24(s, 2H), 4.82(m, 1H), 4.71(d, 1H), 4.12(m, 1H), 3.38(s, 2H), 3.10(dd, 1H), 1.55(m, 2H), 0.90(t, 3H)

Example 275

N-(2,3-Dichlorobenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 8.88(s, 1H), 7.60(d, 2H), 7.45(m, 2H), 7.02-7.50(m, 7H), 6.92(m, 3H), 5.60(d, 1H), 5.28(q, 2H), 4.70(d, 1H), 4.58(m, 1H), 4.03(m, 1H), 3.40(s, 2H), 3.06(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 276

N-(2,3-Dichlorobenzyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.58(s, 1H), 7.60(d, 2H), 7.45(m, 2H), 7.25(m, 3H), 7.10(m, 4H), 6.98(m, 3H), 5.50(d, 1H), 5.25(q, 2H), 4.70(d, 1H), 4.60(m, 1H), 4.04(m, 1H), 3.36(s, 2H), 3.10(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 1H)

Example 277

N-(2,3-Dichlorobenzyl)-N-(4-hydroxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.50(s, 1H), 7.45(d, 1H), 7.18(m, 7H), 7.00(s, 1H), 6.90(d, 2H), 5.50(d, 1H), 5.35(s, 2H), 4.80(d, 1H), 4.50(m, 1H), 4.01(m, 1H), 3.40(s, 2H), 3.18(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.95(t, 3H)

Example 278

N-(2,3-Dichlorobenzyl)-N-(4-isopropylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.18(s, 1H), 7.60(d, 2H), 7.45(m, 2H), 7.20(m, 5H), 7.10(m, 3H), 7.00(s, 2H), 5.40(d, 1H), 5.25(s, 2H), 4.80(m, 1H), 4.68(d, 1H), 4.08(m, 1H), 3.38(s, 2H), 3.08(dd, 1H), 2.90(p, 1H), 1.55(m, 2H), 1.25(d, 6H), 0.92(t, 3H)

Example 279

N-(2,3-Dichlorobenzyl)-N-(2-methoxyethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.52(s, 1H), 7.41(d, 1H), 7.18(m, 4H), 7.00(s, 1H), 6.92(d, 1H), 6.25(bs, 1H), 5.35(q, 2H), 4.90(m, 2H), 4.60(d, 1H), 4.10(m, 1H), 3.78(m, 2H), 3.43(m, 2H), 3.33(s, 2H), 3.20(s, 3H), 3.10(dd, 1H), 1.55(m, 2H), 0.90(t, 3H)

Example 280

N-(2,3-Dichlorobenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.20(d, 1H), 7.65(s, 1H), 7.55(d, 2H), 7.45(m, 2H), 6.90-7.21(m, 7H), 6.80(d, 1H), 5.20(s, 2H), 5.05(m, 2H), 4.75(d, 1H), 4.20(m, 1H), 3.60(s, 3H), 3.38(s, 2H), 3.15(dd, 1H), 1.58(m, 2H), 0.90(t, 3H)

Example 281

N-(2,3-Dichlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.18(s, 1H), 7.60(d, 2H), 7.41(m, 2H), 7.18(m, 6H), 7.00(s, 1H), 6.85(d, 2H), 5.38(m, 1H), 5.26(s, 2H), 4.80(m, 1H), 4.70(d, 1H), 4.10(m, 1H), 3.80(s, 3H), 3.36(s, 2H), 3.07(dd, 1H), 1.55(m, 2H), 0.90(t, 3H)

Example 282

N-(2,3-Dichlorobenzyl)-N-(3-methoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.51(s, 1H), 7.40(d, 2H), 7.20(m, 3H), 7.00(s, 1H), 6.92(s, 1H), 6.85(d, 1H), 5.38(q, 2H), 5.00(t, 1H), 4.60(q,

2H), 4.10(m, 1H), 3.70(m, 2H), 3.40(m, 1H), 3.32(s, 2H), 3.00(dd, 1H), 2.92(s, 3H), 1.75(q, 2H), 1.55(m, 2H), 0.90(t, 3H)

Example 283

N-(2,3-Dichlorobenzyl)-N-(2-methoxypridin-5-ylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.82(s, 1H), 7.78(d, 1H), 7.62(m, 3H), 7.40(m, 2H), 7.25(m, 1H), 7.10(m, 4H), 6.95(s, 1H), 6.70(d, 1H), 5.50(d, 1H), 5.28(q, 2H), 4.70(m, 2H), 4.05(m, 1H), 3.90(s, 3H), 3.38(s, 2H), 3.10(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.92(t, 3H)

Example 284

N-(2,3-Dichlorobenzyl)-N-(methylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.47(s, 1H), 7.40(d, 1H), 7.18(m, 4H), 6.95(m, 2H), 6.70(bs, 1H), 5.35(q, 2H), 5.10(d, 3H), 4.70(m, 1H), 4.58(d, 1H), 4.01(m, 1H), 3.35(s, 2H), 3.12(d, 3H), 3.00(dd, 1H), 1.55(m, 2H), 0.90(t, 3H)

Example 285

N-(2,3-Dichlorobenzyl)-N-(4-methylthiophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.50(s, 1H), 7.60(d, 2H), 7.43(m, 2H), 7.21(m, 4H), 7.10(m, 3H), 6.98(s, 2H), 5.45(d, 1H), 5.2(s, 2H), 4.70(d, 2H), 4.05(m, 1H), 3.38(s, 2H), 3.07(dd, 1H), 2.48(s, 3H), 1.55(m, 2H), 0.90(t, 3H)

Example 286

N-(2,3-Dichlorobenzyl)-N-(2-naphthylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.78(s, 1H), 7.60-7.85(m, 4H), 7.35-7.55(m, 7H), 7.20(m, 2H), 6.97(m, 4H), 5.51(d, 1H), 5.20(q, 2H), 4.72(d, 2H), 4.10(m, 1H), 3.39(s, 2H), 3.10(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 287

N-(2,3-Dichlorobenzyl)-N-(4-nitrophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 9.58(s, 1H), 8.18(d, 2H), 7.75(d, 2H), 7.58(d, 2H), 7.45(m, 2H), 7.41(d, 1H), 7.20(d, 1H), 7.12(t, 4H), 7.00(s, 1H), 6.80(d, 1H), 5.80(d, 1H), 5.28(s, 2H), 4.70(d, 1H), 4.37(m, 1H), 4.00(s, 1H), 3.40(s, 2H), 3.10(dd, 1H), 1.75(m, 1H), 1.55(m, 1H), 0.90(t, 3H)

Example 288

N-(2,3-Dichlorobenzyl)-N-(n-pentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.52(s, 1H), 7.43(d, 1H), 7.18(d, 3H), 7.12(s, 1H), 7.00(s, 1H), 6.95(d, 1H), 6.03(s, 1H), 5.33(q, 2H), 4.90(m, 2H), 4.55(d, 1H), 4.01(m, 1H), 3.65(m, 1H), 3.45(m, 1H), 3.32(s, 2H), 3.00(dd, 1H), 1.55(m, 2H), 1.10(m, 2H), 0.90(m, 5H), 0.85(t, 3H)

Example 289

N-(2,3-Dichlorobenzyl)-N-(phenethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.48(s, 1H), 7.39(d, 1H), 7.18(m, 6H), 7.00(m, 4H), 6.95(d, 1H), 5.97(bs, 1H), 5.31(q, 2H), 4.78(m, 2H), 4.45(d, 1H), 3.98(m, 1H), 3.78(m, 2H), 3.32(s, 2H), 3.00(dd, 1H), 2.85(t, 2H), 1.55(m, 2H), 0.90(t, 3H)

Example 290

N-(2,3-Dichlorobenzyl)-N-(phenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.43(s, 1H), 7.60(d, 2H), 7.45(m, 2H), 7.30(m, 5H), 7.10(m, 4H), 7.009m, 2H), 5.45(d, 1H), 5.25(q, 2H), 4.70(d, 2H), 4.10(m, 1H), 3.38(s, 2H), 3.10(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 291

N-(2,3-Dichlorobenzyl)-N-(n-propylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.50(s, 1H), 7.41(d, 1H), 7.18(m, 4H), 6.97(m, 2H), 6.32(bs, 1H), 5.33(q, 2H), 5.008(d, 1H), 4.75(m, 1H), 4.59(d, 1H), 4.01(m, 1H), 3.59(m, 2H), 3.38(s, 2H), 3.00(dd, 1H), 1.57(m, 4H), 0.90(p, 6H)

Example 292

N-(2,3-Dichlorobenzyl)-N-(3-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.28(s, 1H), 7.60(d, 2H), 7.45(m, 2H), 7.18(d, 2H), 7.10(m, 6H), 7.00(m, 2H), 5.40(d, 1H), 5.25(s, 2H), 4.70(d, 2H), 4.10(m, 1H), 3.39(s, 2H), 3.10(dd, 1H), 2.35(s, 3H), 1.70(m, 1H), 1.50(m, 1H),

0.90(t, 3H)

Example 293

N-(2,3-Dichlorobenzyl)-N-(2-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.82(s, 1H), 7.60(d, 2H), 7.45(m, 2H), 7.05-7.24(m, 7H), 7.00(s, 1H), 5.30(s, 3H), 4.90(m, 1H), 4.74(d, 1H), 4.12(m, 1H), 3.37(s, 2H), 3.10(dd, 1H), 2.12(s, 3H), 1.55(m, 2H), 0.90(t, 3H)

Example 294

N-(2,3-Dichlorobenzyl)-N-(4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 8.22(s, 1H), 7.59(d, 2H), 7.42(m, 2H), 7.10(m, 8H), 7.00(s, 2H), 5.38(d, 1H), 5.25(s, 2H), 4.90(m, 1H), 4.71(d, 1H), 4.10(m, 1H), 3.38(s, 2H), 3.07(dd, 1H), 2.35(s, 3H), 1.60(m, 2H), 0.90(t, 3H)

Example 295

N-(2,3-Dichlorobenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 9.40(s, 1H), 7.82(d, 1H), 7.62(s, 1H), 7.55(d, 2H), 7.42(s, 4H), 7.18(m, 5H), 6.95(s, 1H), 5.78(d, 1H), 5.30(s, 2H), 4.70(d, 1H), 4.43(m, 1H), 4.01(s, 1H), 3.38(s, 2H), 3.10(dd, 1H), 1.75(m, 1H), 1.55(m, 1H), 0.90(t, 3H)

Example 296

N-(2,3-Dichlorobenzyl)-N-(2,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cya

nobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.65(bs, 1H), 7.60(d, 2H), 7.45(m, 2H), 7.18(m, 4H), 7.00(m, 5H), 5.30(m, 3H), 4.90(m, 1H), 4.72(d, 1H), 4.12(m, 1H), 3.38(s, 2H), 3.12(dd, 1H), 2.35(s, 3H), 2.05(s, 3H), 1.60(m, 2H), 0.90(t, 3H)

Example 297

N-(2,3-Dichlorobenzyl)-N-(3,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 8.10(s, 1H), 7.58(d, 2H), 7.45(m, 2H), 7.41(d, 1H), 7.18(m, 5H), 7.00(s, 4H), 5.27(m, 3H), 4.72(m, 2H), 4.10(m, 1H), 3.39(s, 2H), 3.06(dd, 1H), 2.25(s, 6H), 1.60(m, 2H), 0.90(t, 3H)

Example 298

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

<Step 1>

N-(2,3-Dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

Using the same method as described in Preparative Example 3, N-boc-O-benzyl-L-tyrosine was converted to N-boc-O-benzyl-L-tyrosine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid HCl with 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid HCl to give the title compound.

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.57(d, 1H), 7.28-7.43(m, 7H), 7.18-7.20(m, 2H), 6.97-7.03(m, 5H), 6.83(d, 2H), 6.13(d, 1H), 5.04(s, 2H), 4.87(d, 1H), 4.16-4.23(m, 1H), 3.82(d, 2H), 3.27(t, 2H), 2.57-2.73(m, 4H)

<Step 2>

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

To a solution of N-(2,3-Dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine in methylene chloride (0.02M, 1ml, 0.02mmol) was added allylisothiocyanate (0.1M in CH_2Cl_2 , 0.2ml, 0.02mmol). The reaction mixture was agitated for 1hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: methylene chloride/methanol=9/1, v/v) to give the title compound as a white solid.

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.25-7.45(m, 7H), 7.17(t, 2H), 6.85-7.05(m, 7H), 6.75(d, 1H), 6.40(s, 1H), 5.85(m, 1H), 5.15(s, 2H), 5.05(s, 3H), 4.52-4.85(m, 4H), 4.25(t, 3H), 3.50(t, 1H), 3.35(m, 1H), 3.10(m, 1H), 2.85(m, 1H), 2.65(m, 1H)

Examples 299-343

N-(2,3-Dichlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 298 to give the title compounds.

Example 299

N-(2,3-Dichlorobenzyl)-N-(benzylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1

H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 3H), 7.05-7.45(m, 13H), 6.85-7.05(m, 7H), 6.70(m, 2H), 5.05(s, 3H), 4.52-4.90(m, 6H), 4.30(m, 1H), 3.48(t, 1H), 3.30(m, 1H), 3.10(m, 1H), 2.85(m, 1H), 2.65(m, 1H)

Example 300

N-(2,3-Dichlorobenzyl)-N-(2-biphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.70(d, 1H), 7.58(d, 2H), 7.25-7.45(m, 15H), 6.85-7.05(m, 9H), 6.70(m, 2H), 5.05(s, 3H), 4.52-4.80(m, 4H), 4.20(m, 1H), 3.48(t, 1H), 3.32(m, 1H), 3.05(m, 1H), 2.85(m, 1H), 2.60(m, 1H)

Example 301

N-(2,3-Dichlorobenzyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 1H), 7.58(d, 3H), 7.25-7.45(m, 8H), 7.20(m, 4H), 6.85-7.05(m, 7H), 6.65(d, 1H), 5.35(d, 1H), 5.05(s, 2H), 4.65-4.90(m, 4H), 4.50(m, 1H), 3.48(t, 1H), 3.30(m, 1H), 3.18(m, 1H), 2.85(m, 1H), 2.65(m, 1H)

Example 302

N-(2,3-Dichlorobenzyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.75(bs, 1H), 7.58(d, 3H), 7.10-7.50(m, 12H), 6.95(m, 7H), 6.42(d, 1H), 5.60(d, 1H), 5.07(s, 2H), 4.50-4.80(m, 4H), 4.25(m, 1H), 3.48(t, 1H), 3.30(m, 1H), 3.18(m, 1H), 2.95(m, 1H),

2.65(m, 1H)

Example 303

N-(2,3-Dichlorobenzyl)-N-(4-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.60(bs, 1H), 7.58(d, 2H), 7.38-7.50(m, 5H), 7.30(m, 6H), 7.15(m, 2H), 6.95(m, 7H), 6.40(d, 1H), 5.55(d, 1H), 5.05(s, 2H), 4.50-4.80(m, 4H), 4.25(m, 1H), 3.48(t, 1H), 3.30(m, 1H), 3.18(m, 1H), 2.95(m, 1H), 2.65(m, 1H)

Example 304

N-(2,3-Dichlorobenzyl)-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.25-7.45(m, 7H), 7.18(t, 1H), 6.85-7.05(m, 8H), 6.78(d, 1H), 6.22(bs, 1H), 5.50(s, 1H), 5.05(s, 2H), 4.50-4.85(m, 4H), 4.20(m, 3H), 3.65(m, 2H), 3.48(t, 1H), 3.30(m, 1H), 3.05(m, 1H), 2.85(m, 1H), 2.65(m, 1H), 1.30(m, 4H), 0.85(t, 3H)

Example 305

N-(2,3-Dichlorobenzyl)-N-isobutylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.25-7.45(m, 6H), 7.30(m, 6H), 7.17(t, 2H), 6.80-7.05(m, 9H), 6.20(s, 1H), 5.08(s, 2H), 5.00(d, 1H), 4.80(m, 3H), 4.55(m, 1H), 4.25(m, 1H), 3.50(t, 2H), 3.35(m, 2H), 3.10(m, 1H), 2.85(m, 1H), 2.65(m, 1H), 1.90(m, 1H), 0.80(m, 6H)

Example 306

N-(2,3-Dichlorobenzyl)-N-(t-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR (CDCl₃) : δ 7.60(d, 2H), 7.30-7.45(m, 6H), 7.22(m, 2H), 7.15(t, 2H), 7.00(m, 4H), 6.86(m, 3H), 5.38(s, 1H), 5.05(s, 2H), 4.95(d, 2H), 4.60(q, 2H), 4.30(m, 1H), 3.50(t, 1H), 3.33(m, 1H), 3.05(m, 1H), 2.75(d, 2H), 1.40(s, 9H)

Example 307

N-(2,3-Dichlorobenzyl)-N-(2-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 7.95(bs, 1H), 7.65(d, 1H), 7.58(d, 2H), 7.10-7.50(m, 12H), 6.95(m, 7H), 6.62(d, 1H), 5.30(d, 1H), 5.05(s, 2H), 4.65-4.85(m, 4H), 4.45(m, 1H), 3.48(t, 1H), 3.30(m, 1H), 3.18(m, 1H), 2.90(m, 1H), 2.65(m, 1H)

Example 308

N-(2,3-Dichlorobenzyl)-N-(3-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 8.70(bs, 1H), 7.58(d, 2H), 7.45(m, 5H), 7.38(m, 5H), 7.18(m, 3H), 6.95(m, 7H), 6.40(d, 1H), 5.60(d, 1H), 5.07(s, 2H), 4.50-4.85(m, 4H), 4.28(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.95(m, 1H), 2.65(m, 1H)

Example 309

N-(2,3-Dichlorobenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.60(bs, 1H), 7.58(d, 2H), 7.10-7.45(m, 13H), 6.95(m, 7H), 6.42(d, 1H), 5.56(d, 1H), 5.05(s, 2H), 4.50-4.82(m, 4H), 4.25(m, 1H), 3.48(t, 1H), 3.30(m, 1H), 3.18(m, 1H), 2.95(m, 1H), 2.65(m, 1H)

Example 310

N-(2,3-Dichlorobenzyl)-N-(3-chloro-4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.60(bs, 1H), 7.58(d, 2H), 7.10-7.50(m, 13H), 6.95(m, 7H), 6.50(d, 1H), 5.55(d, 1H), 5.07(s, 2H), 4.50-4.85(m, 4H), 4.30(m, 1H), 3.48(t, 1H), 3.32(m, 1H), 3.18(m, 1H), 2.95(m, 1H), 2.65(m, 1H), 2.40(s, 3H)

Example 311

N-(2,3-Dichlorobenzyl)-N-(cyclohexylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.25-7.50(m, 6H), 7.18(t, 2H), 6.80-7.05(m, 7H), 5.90(s, 1H), 5.07(s, 2H), 5.00(d, 1H), 4.80(m, 3H), 4.55(d, 1H), 4.25(m, 2H), 3.50(t, 1H), 3.35(m, 1H), 3.05(m, 1H), 2.85(m, 1H), 2.65(m, 1H), 2.00(m, 2H), 1.30-1.70(m, 6H), 1.10(m, 2H)

Example 312

N-(2,3-Dichlorobenzyl)-N-(cyclopentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.40(m, 6H), 7.15(t, 2H), 6.95(m, 7H), 6.80(d, 1H), 6.05(s, 1H), 5.07(s, 3H), 4.50-4.90(m, 5H), 4.25(m,

1H), 3.48(t, 1H), 3.33(m, 1H), 3.05(m, 1H), 2.85(m, 1H), 2.65(m, 1H), 2.10(m, 2H), 1.55(m, 4H), 1.35(m, 2H)

Example 313

N-(2,3-Dichlorobenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 8.10(bs, 1H), 7.58(d, 3H), 7.10-7.50(m, 11H), 6.95(m, 7H), 6.50(d, 1H), 5.40(d, 1H), 5.07(s, 2H), 4.60-4.80(m, 4H), 4.42(m, 1H), 3.48(t, 1H), 3.30(m, 1H), 3.18(m, 1H), 2.95(m, 1H), 2.65(m, 1H)

Example 314

N-(2,3-Dichlorobenzyl)-N-[(2-dimethylamino)ethylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 7.62(d, 3H), 7.38(m, 7H), 7.08(m, 6H), 6.90(d, 3H), 6.78(s, 1H), 4.90-5.10(m, 2H), 4.60(q, 2H), 4.38(m, 1H), 3.50(m, 2H), 3.25(m, 3H), 2.76(m, 2H), 2.18(m, 2H), 1.98(s, 6H)

Example 315

N-(2,3-Dichlorobenzyl)-N-[(4-dimethylamino)phenylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 7.80(bs, 1H), 7.58(d, 2H), 7.30-7.45(m, 7H), 7.00-7.22(m, 9H), 6.81(m, 3H), 6.65(d, 2H), 5.20(d, 1H), 5.07(s, 2H), 4.85(m, 3H), 4.72(d, 1H), 4.35(m, 1H), 3.48(t, 1H), 3.35(m, 1H), 3.15(m, 1H), 2.95(s, 3H), 2.80(m, 2H)

Example 316

N-(2,3-Dichlorobenzyl)-N-[(3-dimethylamino)propylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 8.90(bs, 1H), 7.63(d, 2H), 7.58(s, 1H), 7.40(m, 7H), 7.10(m, 6H), 6.85(d, 3H), 5.05(m, 5H), 4.52(s, 2H), 4.39(m, 1H), 3.40(m, 3H), 3.25(m, 3H), 3.05(m, 1H), 2.75(m, 2H), 2.40(m, 2H), 1.90(s, 6H)

Example 317

N-(2,3-Dichlorobenzyl)-N-(ethoxycarbonylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 7.62(d, 2H), 7.40(m, 7H), 6.98-7.20(m, 8H), 6.929m, 2H), 6.42(bs, 1H), 5.07(s, 2H), 4.85(m, 3H), 4.609d, 1H), 4.35(m, 1H), 4.20(q, 1H), 3.48(t, 1H), 3.30(m, 1H), 3.08(m, 1H), 2.95(m, 1H), 2.65(m, 1H), 1.30(t, 3H)

Example 318

N-(2,3-Dichlorobenzyl)-N-(3-ethoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 7.62(d, 2H), 7.40(m, 7H), 7.08(m, 7H), 6.85(m, 4H), 5.07(s, 2H), 4.98(m, 3H), 4.60(q, 2H), 4.30(m, 1H), 3.759d, 2H), 3.44(m, 4H), 3.25(m, 4H), 3.05(m, 1H), 2.75(d, 2H), 1.80(m, 2H), 0.92(t, 3H)

Example 319

N-(2,3-Dichlorobenzyl)-N-(ethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.25-7.45(m, 7H), 7.17(t, 1H), 6.87-7.05(m, 8H), 6.75(d, 1H), 6.35(s, 1H), 5.20(d, 1H), 5.05(s, 2H), 4.80(q, 2H), 4.60(d, 2H), 4.25(t, 3H), 4.67(p, 2H), 3.50(t, 1H), 3.35(m, 1H), 3.05(m, 1H), 2.85(m, 1H), 2.65(m, 1H), 1.18(t, 3H)

Example 320

N-(2,3-Dichlorobenzyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.00(bs, 1H), 7.58(d, 2H), 7.40(m, 4H), 7.30(m, 5H), 7.18(m, 4H), 6.95(m, 7H), 6.62(d, 1H), 5.36(d, 1H), 5.07(s, 2H), 4.78(m, 4H), 4.40(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.90(m, 1H), 2.65(m, 1H)

Example 321

N-(2,3-Dichlorobenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.65(bs, 1H), 7.58(d, 2H), 7.42(m, 3H), 7.30(m, 6H), 7.19(m, 3H), 6.95(m, 8H), 6.42(d, 1H), 5.60(d, 1H), 5.07(s, 2H), 4.78(m, 3H), 4.60(m, 1H), 4.30(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.95(m, 1H), 2.65(m, 1H)

Example 322

N-(2,3-Dichlorobenzyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.42(bs, 1H), 7.58(d, 2H), 7.42(m, 4H), 7.30(m, 5H), 7.10(m, 4H), 6.95(m, 7H), 6.50(d, 1H), 5.50(d, 1H), 5.07(s, 2H), 4.70(m, 4H), 4.30(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.95(m, 1H), 2.65(m, 1H)

Example 323

N-(2,3-Dichlorobenzyl)-N-(4-hydroxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.10(bs, 1H), 7.58(d, 2H), 7.38(m, 7H), 7.18(t, 2H), 6.95(m, 10H), 6.68(d, 2H), 5.16(d, 1H), 5.05(s, 2H), 4.90(m, 3H), 4.62(d, 1H), 4.38(bs, 1H), 3.48(t, 1H), 3.33(t, 1H), 3.11(m, 1H), 2.77(d, 2H)

Example 324

N-(2,3-Dichlorobenzyl)-N-(4-isopropylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.13(bs, 1H), 7.58(d, 2H), 7.41(m, 3H), 7.30(m, 5H), 7.20(s, 4H), 7.15(m, 2H), 6.95(m, 6H), 6.70(d, 1H), 5.38(d, 1H), 5.07(s, 2H), 4.78(m, 4H), 4.30(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.90(m, 1H), 2.65(m, 1H)

Example 325

N-(2,3-Dichlorobenzyl)-N-(2-methoxyethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.14(bs, 1H), 7.7.60(m, 2H), 7.38(m, 5H), 7.20(m, 3H), 6.95(m, 7H), 6.70(d, 1H), 6.28(s, 1H), 5.36(d, 1H), 5.07(d, 2H), 4.85(m, 3H), 4.60(m, 1H), 4.30(m, 1H), 3.80(m, 1H), 3.48(m, 2H),

3.33(m, 1H), 3.18(m, 3H), 2.90(m, 1H), 2.70(m, 1H), 1.12(d, 3H)

Example 326

N-(2,3-Dichlorobenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyano benzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 8.20(d, 1H), 7.60(m, 3H), 7.38(m, 7H), 7.18(m, 2H), 7.00(m, 7H), 6.90(m, 4H), 5.15(d, 1H), 5.05(s, 2H), 4.92(m, 3H), 4.70(d, 1H), 4.45(m, 1H), 3.60(s, 3H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.80(d, 2H)

Example 327

N-(2,3-Dichlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyano benzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 8.10(bs, 1H), 7.58(d, 3H), 7.40(m, 7H), 7.20(m, 4H), 6.95(m, 8H), 6.75(d, 1H), 5.36(d, 1H), 5.07(s, 2H), 4.78(m, 4H), 4.32(m, 1H), 3.80(s, 3H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.90(m, 1H), 2.65(m, 1H)

Example 328

N-(2,3-Dichlorobenzyl)-N-(3-methoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyano benzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 7.61(d, 2H), 7.38(m, 8H), 7.05(m, 6H), 6.90(s, 2H), 6.82(m, 2H), 5.00(m, 5H), 4.58(q, 2H), 4.32(m, 1H), 3.70(m, 2H), 3.48(t, 1H), 3.38(m, 3H), 3.08(m, 1H), 2.92(s, 3H), 2.75(d, 2H)

Example 329

N-(2,3-Dichlorobenzyl)-N-(2-methoxypyridin-5-ylthiocarbamoyl)-2(S)-{[1-(4-

cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 8.60(bs, 1H), 8.00(s, 1H), 7.63(m, 1H), 7.58(d, 2H), 7.40(m, 3H), 7.07-7.37(m, 7H), 6.95(m, 6H), 6.72(d, 1H), 6.58(d, 1H), 5.52(d, 1H), 5.07(s, 2H), 4.78(m, 4H), 4.31(m, 1H), 3.90(s, 3H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.95(m, 1H), 2.65(m, 1H)

Example 330

N-(2,3-Dichlorobenzyl)-N-(methylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 7.61(d, 2H), 7.40(m, 8H), 7.15(t, 1H), 6.95(m, 8H), 6.70(d, 1H), 5.20(d, 1H), 5.07(s, 2H), 4.80(q, 2H), 4.60(m, 2H), 4.21(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.13(d, 3H), 3.05(m, 1H), 2.90(m, 1H), 2.65(m, 1H)

Example 331

N-(2,3-Dichlorobenzyl)-N-(4-methylthiophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 8.40(bs, 1H), 7.58(d, 2H), 7.42(m, 4H), 7.25(m, 8H), 7.18(m, 2H), 6.95(m, 6H), 6.60(d, 1H), 5.42(d, 1H), 5.07(s, 2H), 4.70(m, 4H), 4.30(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.92(m, 1H), 2.70(m, 1H), 2.45(s, 3H)

Example 332

N-(2,3-Dichlorobenzyl)-N-(2-naphthylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.60(bs, 1H), 7.78(m, 4H), 7.15-7.55(m, 15H), 6.95(m, 6H), 6.60(d, 1H), 5.50(d, 1H), 5.07(s, 2H), 4.78(m, 4H), 4.40(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.90(m, 1H), 2.65(m, 1H)

Example 333

N-(2,3-Dichlorobenzyl)-N-(4-nitrophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 9.40(s, 1H), 8.20(d, 2H), 7.78(d, 2H), 7.58(d, 2H), 7.15-7.45(m, 10H), 6.95(m, 6H), 6.28(d, 1H), 5.80(d, 1H), 5.07(s, 2H), 4.80(d, 1H), 4.62(q, 2H), 4.40(m, 1H), 4.20(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.11(m, 1H), 3.00(m, 1H), 2.65(m, 1H)

Example 334

N-(2,3-Dichlorobenzyl)-N-(n-pentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.40(m, 8H), 7.15(t, 1H), 7.00(m, 5H), 6.88(m, 3H), 6.12(s, 1H), 5.07(s, 2H), 4.99(d, 1H), 4.80(m, 3H), 4.59(d, 1H), 4.30(m, 1H), 3.65(m, 1H), 3.48(t, 1H), 3.33(m, 2H), 3.11(m, 1H), 2.85(m, 1H), 2.65(m, 1H), 1.70(m, 2H), 1.10(m, 2H), 0.80(m, 5H)

Example 335

N-(2,3-Dichlorobenzyl)-N-(phenethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.40(m, 7H), 7.18(m, 3H), 6.85-7.10(m, 11H), 6.76(d, 1H), 5.95(s, 1H), 5.07(s, 2H), 4.80(m, 4H), 4.42(d, 1H), 4.24(m, 1H), 3.85(m, 2H), 3.48(t, 1H), 3.33(m, 1H), 3.03(m, 1H), 2.82(t, 2H), 2.70(m, 2H)

Example 336

N-(2,3-Dichlorobenzyl)-N-(phenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 8.30(bs, 1H), 7.58(d, 2H), 7.20-7.45(m, 13H), 7.18(m, 2H), 6.95(m, 6H), 6.62(d, 1H), 5.41(d, 1H), 5.07(s, 2H), 4.73(m, 4H), 4.32(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.90(m, 1H), 2.65(m, 1H)

Example 337

N-(2,3-Dichlorobenzyl)-N-(n-propylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 7.62(d, 2H), 7.42(m, 4H), 7.32(m, 3H), 7.18(t, 1H), 7.00(m, 6H), 6.90(m, 2H), 6.79(d, 1H), 6.30(s, 1H), 5.15(d, 1H), 5.07(s, 2H), 4.80(q, 2H), 4.58(d, 2H), 4.25(m, 1H), 3.51(m, 3H), 3.33(m, 1H), 3.08(m, 1H), 2.90(m, 1H), 2.65(m, 1H), 1.55(q, 2H), 0.85(t, 3H)

Example 338

N-(2,3-Dichlorobenzyl)-N-(3-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 8.12(bs, 1H), 7.58(d, 2H), 7.42(m, 3H), 7.32(m, 4H), 7.18(m, 6H), 6.95(m, 7H), 6.65(d, 1H), 5.40(d, 1H), 5.07(s, 2H), 4.78(m, 4H), 4.35(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.90(m, 1H), 2.65(m, 1H), 2.32(s, 3H)

Example 339

N-(2,3-Dichlorobenzyl)-N-(2-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

enzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR (CDCl₃) : δ 7.68(bs, 1H), 7.58(d, 2H), 7.42(m, 3H), 7.30(m, 4H), 7.19(m, 5H), 6.95(m, 9H), 5.25(d, 1H), 5.07(s, 2H), 4.79(m, 4H), 4.40(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.85(m, 1H), 2.75(m, 1H), 2.12(s, 3H)

Example 340

N-(2,3-Dichlorobenzyl)-N-(4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR(CDCl₃) : δ 8.15(bs, 1H), 7.58(d, 2H), 7.38(m, 7H), 7.18(s, 6H), 6.95(m, 7H), 6.70(d, 1H), 5.36(d, 1H), 5.07(s, 2H), 4.79(m, 4H), 4.36(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.85(m, 1H), 2.70(m, 1H), 2.34(s, 3H)

Example 341

N-(2,3-Dichlorobenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

¹H-NMR (CDCl₃) : δ 9.02(bs, 1H), 7.72(m, 2H), 7.40-7.55(m, 7H), 7.11-7.38(m, 6H), 6.95(m, 7H), 6.40(d, 1H), 5.70(d, 1H), 5.07(s, 2H), 4.71(m, 3H), 4.52(m, 1H), 4.28(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.20(m, 1H), 3.00(m, 1H), 2.65(m, 1H)

Example 342

N-(2,3-Dichlorobenzyl)-N-(2,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.58(d, 3H), 7.25-7.50(m, 8H), 7.18(m, 2H), 7.00(m, 7H), 6.88(m, 3H), 5.21(d, 1H), 5.07(s, 2H), 4.79(m, 4H), 4.40(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.85(m, 1H), 2.75(m, 1H), 2.31(s, 3H), 2.10(s, 3H)

Example 343

N-(2,3-Dichlorobenzyl)-N-(3,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.00(bs, 1H), 7.58(d, 2H), 7.42(m, 3H), 7.32(m, 4H), 7.15(m, 3H), 6.95(m, 9H), 6.72(d, 1H), 5.32(d, 1H), 5.07(s, 2H), 4.79(m, 4H), 4.37(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.18(m, 1H), 2.85(m, 1H), 2.75(m, 1H), 2.25(s, 6H)

Example 344

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

<Step 1>

N-(2,3-Dichlorobenzyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

Using the same method as described in Preparative Example 3, N-boc-glycine was converted to N-boc-glycine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid HCl with 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid HCl to give the title compound.

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.53(s, 1H), 7.38(dd, 1H),

7.13-7.21(m, 4H), 6.98(s, 1H), 6.61(bs, 1H), 5.27(s, 2H), 3.84(s, 2H), 3.36(s, 2H), 3.25(q, 2H), 2.70(t, 2H)

<Step 2>

N-(2,3-Dichlorobenzyl)-N-(allylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

To a solution of N-(2,3-dichlorobenzyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine in methylene chloride (0.02M, 1ml, 0.02mmol) was added allylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 1hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: methylene chloride/methanol=9/1, v/v) to give the title compound as a white solid.

¹H-NMR(CDCl₃) : δ 7.63(d, 2H), 7.51(s, 1H), 7.42(d, 1H), 7.25(d, 1H), 7.16(d, 2H), 7.04(d, 1H), 6.96(s, 1H), 6.66(bs, 1H), 5.80-5.96(m, 1H), 5.27(s, 2H), 5.12(dd, 2H), 4.94(d, 2H), 4.30(t, 2H), 3.29-3.39(m, 4H)

Examples 345-387

N-(2,3-Dichlorobenzyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 344 to give the title compounds.

Example 345

N-(2,3-Dichlorobenzyl)-N-(benzylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.58(d, 2H), 7.45(s, 1H), 7.40(d, 1H), 7.03-7.32(m, 9H), 6.91(s, 1H), 5.12(s, 2H), 4.94(d, 2H), 4.88(d, 2H), 3.85(t, 2H), 3.29-3.37(m, 4H)

Example 346

N-(2,3-Dichlorobenzyl)-N-(2-biphenylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-5-yl}] \text{acetyl}\}$ aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.99(bs, 1H), 7.62(d, 1H), 7.57(d, 2H), 7.46(s, 1H), 7.29-7.42(m, 8H), 7.16(d, 2H), 7.04(d, 2H), 6.91(s, 1H), 5.77(d, 1H), 5.18(s, 2H), 4.86(s, 2H), 3.72(t, 2H), 3.29(s, 2H), 3.18-3.25(m, 2H)

Example 347

N-(2,3-Dichlorobenzyl)-N-(2-bromophenylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-5-yl}] \text{acetyl}\}$ aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.17(bs, 1H), 7.53-7.67(m, 4H), 7.43-7.46(m, 2H), 7.29-7.38(m, 3H), 7.09-7.19(m, 3H), 6.95(s, 1H), 5.21(s, 2H), 5.07(s, 2H), 3.96(t, 2H), 3.43-3.52(m, 2H), 3.36(s, 2H)

Example 348

N-(2,3-dichlorobenzyl)-N-(3-bromophenylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-5-yl}] \text{acetyl}\}$ aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 9.11(bs, 1H), 7.40-7.59(m, 6H), 7.15-7.32(m, 4H), 7.09(d, 2H), 6.92(s, 1H), 5.24(s, 2H), 5.19(s, 2H), 3.72(t, 2H), 3.32-3.37(m, 4H)

Example 349

N-(2,3-Dichlorobenzyl)-N-(4-bromophenylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-5-yl}] \text{acetyl}\}$ aminoethylamine

yl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR(CDCl₃) : δ 8.91(bs, 1H), 7.57(d, 2H), 7.40-7.46(m, 4H), 7.34(s, 1H), 7.19-7.30(m, 3H), 7.07(d, 2H), 6.92(s, 1H), 5.19(s, 2H), 5.18(s, 2H), 3.73(t, 2H), 3.32-3.37(m, 4H)

Example 350

N-(2,3-Dichlorobenzyl)-N-(n-butylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR(CDCl₃) : δ 7.64(d, 2H), 7.52(s, 1H), 7.41(d, 1H), 7.13-7.23(m, 3H), 7.04(d, 1H), 6.98(s, 1H), 6.50(bs, 1H), 5.28(s, 2H), 4.93(s, 2H), 3.81(t, 2H), 3.62(q, 2H), 3.36(s, 2H), 3.27-3.33(m, 2H), 1.49-1.60(m, 2H), 1.22-1.30(m, 2H), 0.89(t, 3H)

Example 351

N-(2,3-Dichlorobenzyl)-N-(isobutylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR(CDCl₃) : δ 7.64(d, 2H), 7.52(s, 1H), 7.42(d, 1H), 7.14-7.24(m, 3H), 7.05(d, 1H), 6.98(s, 1H), 6.45(bs, 1H), 5.28(s, 2H), 4.92(s, 2H), 3.85(t, 2H), 3.45(t, 2H), 3.36(s, 2H), 3.29-3.32(m, 2H), 1.91-1.94(m, 1H), 0.84(d, 6H)

Example 352

N-(2,3-Dichlorobenzyl)-N-(t-butylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR(CDCl₃) : δ 7.64(d, 2H), 7.55(s, 1H), 7.44(d, 1H), 7.15-7.32(m, 3H), 7.03(s, 1H), 6.97(d, 1H), 5.55(bs, 1H), 5.30(s, 2H), 4.76(s, 2H),

3.99(t, 2H), 3.86-3.36(m, 2H), 3.36(s, 2H), 1.43(s, 9H)

Example 353

N-(2,3-Dichlorobenzyl)-N-(2-chlorophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.20(bs, 1H), 7.56-7.67(m, 3H), 7.40-7.46(m, 3H), 7.08-7.37(m, 6H), 6.95(s, 1H), 5.21(s, 2H), 5.07(s, 2H), 3.96(t, 2H), 3.42-3.50(m, 2H), 3.36(s, 2H)

Example 354

N-(2,3-Dichlorobenzyl)-N-(3-chlorophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(d, 2H), 7.47(s, 1H), 7.37-7.45(m, 3H), 7.12-7.29(m, 6H), 6.95(s, 1H), 5.33(s, 2H), 5.23(s, 2H), 3.68-3.78(m, 4H), 3.37(m, 2H)

Example 355

N-(2,3-Dichlorobenzyl)-N-(4-chlorophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.85(bs, 1H), 7.57(d, 2H), 7.40-7.55(m, 3H), 7.21-7.35(m, 4H), 6.99-7.10(m, 3H), 6.94(s, 1H), 5.20(s, 2H), 5.18(s, 2H), 3.74(t, 2H), 3.33-3.37(m, 4H)

Example 356

N-(2,3-Dichlorobenzyl)-N-(3-chloro-4-methylphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.89(bs, 1H), 7.57(d, 2H), 7.46(s, 1H), 7.37-7.43(m, 2H), 7.20-7.27(m, 3H), 7.08-7.15(m, 3H), 6.93(s, 1H), 5.23(s, 2H), 5.17(s, 2H), 3.75(t, 2H), 3.32-3.38(m, 4H), 2.34(s, 3H)

Example 357

N-(2,3-Dichlorobenzyl)-N-(cyclohexylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.64(d, 2H), 7.55(s, 1H), 7.42(d, 1H), 7.01-7.23(m, 5H), 6.14(bs, 1H), 5.29(s, 2H), 4.91(s, 2H), 4.25-4.33(m, 1H), 3.81(t, 2H), 3.37(s, 2H), 3.26-3.31(m, 2H), 1.96-2.02(m, 2H), 1.63(bs, 2H), 1.05-1.35(m, 6H)

Example 358

N-(2,3-Dichlorobenzyl)-N-(cyclopentylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.64(d, 2H), 7.54(s, 1H), 7.42(d, 1H), 6.99-7.23(m, 5H), 6.37(bs, 1H), 5.29(s, 2H), 4.95(s, 2H), 4.70(q, 1H), 3.77(t, 2H), 3.37(s, 2H), 3.25-3.31(m, 2H), 1.98-2.11(m, 2H), 1.53-1.63(m, 4H), 1.37-1.50(m, 2H)

Example 359

N-(2,3-Dichlorobenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.30(bs, 1H), 7.55-7.62(m, 3H), 7.47(s, 1H), 7.41(dd, 1H), 7.16-7.30(m, 3H), 7.12(d, 2H), 6.98(bs, 1H), 6.94(s, 1H), 5.21(s, 2H), 5.09(s, 2H), 3.31(t, 2H), 3.44(q, 2H), 3.36(s, 2H)

Example 360

N-(2,3-Dichlorobenzyl)-N-(4-dimethylaminophenylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR(CDCl₃) : δ 8.11(bs, 1H), 7.56(d, 2H), 7.46(s, 1H), 7.43(d, 1H), 7.25(d, 2H), 7.10(d, 3H), 6.96(s, 1H), 6.25(d, 1H), 5.22(s, 2H), 5.05(s, 2H), 3.91(t, 2H), 3.42(q, 2H), 3.35(s, 2H), 2.93(s, 6H)

Example 361

N-(2,3-Dichlorobenzyl)-N-(ethoxycarbonylmethylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR(CDCl₃) : δ 7.64(d, 2H), 7.50(s, 1H), 7.41(dd, 1H), 7.05-7.24(m, 4H), 6.97(s, 1H), 5.26(s, 2H), 4.96(s, 2H), 4.38(d, 2H), 4.18(q, 2H), 3.85(t, 2H), 3.41-3.44(m, 2H), 3.38(s, 2H), 1.27(t, 3H)

Example 362

N-(2,3-Dichlorobenzyl)-N-(3-ethoxypropylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR(CDCl₃) : δ 7.64(d, 2H), 7.54(s, 1H), 7.42(d, 2H), 7.15-7.23(m, 2H), 7.02(s, 1H), 6.03(d, 1H), 5.31(s, 2H), 4.72(s, 2H), 3.98(t, 2H), 3.71(q, 2H), 3.38-3.47(m, 4H), 3.36(s, 2H), 3.24(q, 2H), 1.77-1.83(m, 2H), 0.92(t, 3H)

Example 363

N-(2,3-Dichlorobenzyl)-N-(ethylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR(CDCl₃) : δ 7.64(d, 2H), 7.53(s, 1H), 7.41(d, 1H), 7.03-7.24(m,

4H), 6.98(s, 1H), 6.56(bs, 1H), 5.28(s, 2H), 4.94(s, 2H), 3.78(t, 2H), 3.65(q, 2H), 3.37(s, 2H), 3.31(q, 2H), 1.91(t, 3H)

Example 364

N-(2,3-Dichlorobenzyl)-N-(2-fluorophenylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]aminoethylamine

¹H-NMR(CDCl₃) : δ 8.30(bs, 1H), 7.58(d, 2H), 7.41-7.51(m, 3H), 7.03-7.29(m, 8H), 6.94(s, 1H), 5.21(s, 2H), 5.10(s, 2H), 3.90(t, 2H), 3.41(q, 2H), 3.36(s, 2H)

Example 365

N-(2,3-Dichlorobenzyl)-N-(3-fluorophenylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]aminoethylamine

¹H-NMR(CDCl₃) : δ 8.98(bs, 1H), 7.57(d, 2H), 7.47(s, 1H), 7.40-7.45(m, 1H), 7.22-7.30(m, 6H), 7.09(d, 2H), 6.93(s, 1H), 6.85-6.91(m, 1H), 5.22(s, 2H), 5.20(s, 2H), 3.78(t, 2H), 3.30-3.36(m, 2H), 3.38(s, 2H)

Example 366

N-(2,3-Dichlorobenzyl)-N-(4-fluorophenylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]aminoethylamine

¹H-NMR(CDCl₃) : δ 8.68(bs, 1H), 7.58(d, 2H), 7.41-7.47(m, 1H), 7.19-7.37(m, 6H), 7.08(d, 2H), 7.02(s, 1H), 6.94(s, 1H), 5.20(s, 2H), 5.15(s, 2H), 3.78(t, 2H), 3.37(s, 2H), 3.34(q, 2H)

Example 367

N-(2,3-Dichlorobenzyl)-N-(4-hydroxyphenylthiocarbamoyl)-2-[[1-(4-cyanobe

nzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR(CD₃OD) δ : 7.74(s, 1H), 7.64(d, 2H), 7.48(d, 1H), 7.32(t, 1H), 7.22(d, 2H), 7.14(d, 1H), 7.08(d, 2H), 6.95(s, 1H), 6.72(d, 2H), 5.35(s, 2H), 5.14(s, 2H), 3.76(t, 2H), 3.31-3.43(m, 2H), 3.30(s, 2H)

Example 368

N-(2,3-Dichlorobenzyl)-N-(4-isopropylphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR(CDCl₃) : δ 8.39(bs, 1H), 7.56(d, 2H), 7.47(s, 1H), 7.39-7.46(m, 1H), 7.11-7.31(m, 5H), 7.03(d, 2H), 6.96(s, 1H), 5.21(s, 2H), 5.12(s, 2H), 3.84(t, 2H), 3.36(bs, 4H), 2.83-2.96(m, 1H), 1.23(d, 6H)

Example 369

N-(2,3-Dichlorobenzyl)-N-(2-methoxyethylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR(CDCl₃) : δ 7.64(d, 2H), 7.54(s, 1H), 7.43(d, 1H), 7.16-7.23(m, 3H), 7.01(s, 1H), 6.98(d, 1H), 6.41(bs, 1H), 5.29(s, 2H), 4.83(s, 2H), 3.95(t, 2H), 3.79(q, 2H), 3.40-3.50(m, 4H), 3.36(s, 2H), 3.21(s, 3H)

Example 370

N-(2,3-Dichlorobenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR(CDCl₃) : δ 8.14(d, 1H), 7.45-7.61(m, 5H), 7.20-7.28(m, 2H), 7.09-7.16(m, 3H), 7.01(s, 1H), 6.81(d, 1H), 5.23(s, 2H), 4.29(s, 2H), 4.14(t, 2H), 3.60(s, 3H), 3.52(q, 2H), 3.37(s, 2H)

Example 371

N-(2,3-Dichlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.38(bs, 1H), 7.57(d, 2H), 7.46(s, 1H), 7.41-7.45(m, 1H), 7.16-7.14(m, 4H), 7.09(d, 2H), 6.95(s, 1H), 6.85(d, 2H), 5.21(s, 2H), 5.10(s, 2H), 3.85(t, 2H), 3.79(s, 3H), 3.37(q, 2H), 3.36(s, 2H)

Example 372

N-(2,3-Dichlorobenzyl)-N-(3-methoxypropylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.64(d, 2H), 7.54(s, 1H), 7.43(d, 1H), 7.16-7.23(m, 3H), 7.03(s, 1H), 6.91(bs, 1H), 6.89(d, 1H), 5.31(s, 2H), 4.67(s, 2H), 4.02(t, 2H), 3.66(q, 2H), 3.38-3.45(m, 4H), 3.36(s, 2H), 2.94(s, 3H), 1.74-1.80(m, 2H)

Example 373

N-(2,3-Dichlorobenzyl)-N-(2-methoxy-pyridin-5ylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.86(bs, 1H), 8.01(d, 1H), 7.71(dd, 1H), 7.59(d, 2H), 7.45(s, 1H), 7.41-7.44(m, 1H), 7.19-7.28(m, 2H), 7.10(d, 2H), 6.93(s, 1H), 6.73(d, 2H), 5.21(s, 2H), 5.17(s, 2H), 3.90(s, 3H), 3.80(t, 2H), 3.36(bs, 4H)

Example 374

N-(2,3-Dichlorobenzyl)-N-(methylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-i

imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.64(d, 2H), 7.51(s, 1H), 7.41(d, 1H), 7.15-7.23(m, 3H), 7.04(d, 1H), 6.97(d, 1H), 6.78(bs, 1H), 5.27(s, 2H), 4.93(s, 2H), 3.79(t, 2H), 3.37(s, 2H), 3.27-3.37(m, 2H), 3.11(d, 2H)

Example 375

N-(2,3-Dichlorobenzyl)-N-(4-methylthiophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.67(bs, 1H), 7.56(d, 2H), 7.46(s, 1H), 7.41-7.45(m, 1H), 7.18-7.49(m, 5H), 7.08(d, 2H), 6.94(s, 1H), 5.20(s, 2H), 5.14(s, 2H), 3.78(t, 2H), 3.37(bs, 4H), 2.46(s, 3H)

Example 376

N-(2,3-Dichlorobenzyl)-N-(2-naphthylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.93(bs, 1H), 7.69-7.80(m, 3H), 7.58(dd, 1H), 7.41-7.48(m, 5H), 7.23-7.30(m, 2H), 7.06-7.12(m, 1H), 6.94-7.00(m, 3H), 5.16(s, 2H), 5.14(s, 2H), 3.78(t, 2H), 3.34(bs, 4H)

Example 377

N-(2,3-Dichlorobenzyl)-N-(4-nitrophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 9.52(bs, 1H), 8.17(d, 2H), 7.83(d, 2H), 7.53-7.59(m, 3H), 7.42-7.46(m, 1H), 7.24-7.27(m, 2H), 7.09(d, 2H), 6.97(s, 1H), 6.82-6.89(m, 1H), 5.29(s, 2H), 5.21(s, 2H), 3.65(t, 2H), 3.44(s, 2H), 3.30-3.34(m, 2H)

Example 378

N-(2,3-Dichlorobenzyl)-N-(n-pentylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.64(d, 2H), 7.53(s, 1H), 7.42(d, 1H), 7.02-7.23(m, 4H), 6.99(s, 1H), 6.29(bs, 1H), 5.28(s, 2H), 4.89(s, 2H), 3.88(t, 2H), 3.43-3.61(m, 2H), 3.36(bs, 4H), 1.67-1.74(m, 1H), 1.04-1.29(m, 2H), 0.78-0.89(m, 5H)

Example 379

N-(2,3-Dichlorobenzyl)-N-(phenethylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.62(d, 2H), 7.50(s, 1H), 7.38(d, 1H), 7.11-7.17(m, 6H), 6.99-7.07(m, 3H), 6.84(d, 1H), 6.07(bs, 1H), 5.27(s, 2H), 4.69(s, 2H), 3.81-3.90(m, 4H), 3.28-3.34(m, 4H), 2.86(t, 3H)

Example 380

N-(2,3-Dichlorobenzyl)-N-(phenylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.57(bs, 1H), 7.55(d, 2H), 7.47(s, 1H), 7.33-7.45(m, 5H), 7.17-7.29(m, 3H), 7.08(d, 2H), 6.95(s, 1H), 5.20(s, 2H), 5.14(s, 2H), 3.82(t, 2H), 3.37(bs, 4H)

Example 381

N-(2,3-Dichlorobenzyl)-N-(n-propylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.64(d, 2H), 7.53(s, 1H), 7.42(d, 1H), 7.02-7.23(m, 4H), 6.99(s, 1H), 6.46(bs, 1H), 5.28(s, 2H), 4.92(s, 2H), 3.81(t, 2H), 3.54-3.64(m, 2H), 3.36(s, 2H), 3.27-3.33(m, 2H), 1.55-1.65(m, 2H), 0.87(t, 3H)

Example 382

N-(2,3-Dichlorobenzyl)-N-(3-methylphenylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-5-yl]acetyl}\}$ aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.43(bs, 1H), 7.56(d, 2H), 7.47(s, 1H), 7.41-7.45(m, 1H), 7.01-7.29(m, 8H), 6.96(s, 1H), 5.21(s, 2H), 5.12(s, 2H), 3.83(t, 2H), 3.37(bs, 4H), 2.33(s, 3H)

Example 383

N-(2,3-Dichlorobenzyl)-N-(2-methylphenylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-5-yl]acetyl}\}$ aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.02(bs, 1H), 7.57(d, 2H), 7.47(s, 1H), 7.43-7.46(m, 1H), 7.20-7.30(m, 6H), 7.10(d, 2H), 6.94(s, 1H), 5.21(s, 2H), 5.07(s, 2H), 3.93(t, 2H), 3.39-3.42(m, 2H), 3.34(s, 2H), 2.15(s, 3H)

Example 384

N-(2,3-Dichlorobenzyl)-N-(4-methylphenylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-5-yl]acetyl}\}$ aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.44(bs, 1H), 7.56(d, 2H), 7.46(s, 1H), 7.41-7.44(m, 1H), 7.07-7.28(m, 8H), 6.95(s, 1H), 5.21(s, 2H), 5.11(s, 2H), 3.84(t, 2H), 3.37-3.39(m, 2H), 3.36(s, 2H), 2.34(s, 3H)

Example 385

N-(2,3-Dichlorobenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 9.33(bs, 1H), 7.85-7.89(m, 1H), 7.69(s, 1H), 7.56(d, 2H), 7.38-7.59(m, 3H), 7.24-7.28(m, 2H), 7.05-7.14(m, 3H), 6.92(s, 1H), 5.24(s, 4H), 3.72(t, 2H), 3.37(bs, 4H)

Example 386

N-(2,3-Dichlorobenzyl)-N-(2,4-dimethylphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.91(bs, 1H), 7.57(d, 2H), 7.47(s, 1H), 7.42-7.46(m, 1H), 7.20-7.30(m, 3H), 7.15(d, 2H), 7.01(s, 2H), 6.94(s, 1H), 5.22(s, 2H), 5.05(s, 2H), 3.94(t, 2H), 3.40-3.45(m, 2H), 3.34(s, 2H), 2.30(s, 3H), 2.11(s, 3H)

Example 387

N-(2,3-Dichlorobenzyl)-N-(3,4-dimethylphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.33(bs, 1H), 7.56(d, 2H), 7.47(s, 1H), 7.41-7.45(m, 1H), 7.08-7.29(m, 7H), 6.96(s, 1H), 5.21(s, 2H), 5.09(s, 2H), 3.85(t, 2H), 3.40-3.43(m, 2H), 3.36(s, 2H), 2.22(s, 6H)

Example 388

N-(1-Naphthylmethyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of N-(1-naphthylmethyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine in dichloromethane

(0.02M, 1ml, 0.02mmol) was added allylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated overnight at room temperature. The mixture was purified by silica gel column chromatography(eluent: CH₂Cl₂ /MeOH=9/1, v/v) to give the title compound as a white solid.

¹H-NMR (CDCl₃) : δ 7.02-8.20(m, 13H), 5.65(m, 2H), 5.22-5.40(m, 4H), 5.00(m, 2H), 4.22(bs, 2H), 3.35(s, 2H), 3.10(dd, 1H), 1.60(m, 1H), 1.42(bs, 1H), 0.85-1.15(m, 7H)

Examples 389-417

N-(1-Naphthylmethyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine was reacted with the corresponding isothiocyanates under the same condition as described in Example 388 to give the title compounds.

Example 389

N-(1-Naphthylmethyl)-N-benzylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.02-8.20(m, 18H), 5.95(t, 1H), 5.30(m, 3H), 5.02(m, 2H), 4.80(d, 2H), 4.22(bs, 1H), 3.28(s, 2H), 3.15(dd, 1H), 1.60(m, 1H), 1.42(bs, 1H), 0.85-1.15(m, 7H)

Example 390

N-(1-Naphthylmethyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.02-8.18(m, 17H), 5.10-5.45(m, 5H), 4.35(m,

1H), 3.40(d, 2H), 3.22(dd, 2H), 1.60(m, 1H), 1.42(bs, 1H), 0.85-1.15(m, 7H)

Example 391

N-(1-Naphthylmethyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.02-8.18(m, 17H), 5.10-5.40(m, 5H), 4.25(m, 1H), 3.38(s, 2H), 3.20(dd, 2H), 1.60(m, 1H), 1.40(bs, 1H), 0.80-1.10(m, 7H)

Example 392

N-(1-Naphthylmethyl)-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-8.20(m, 13H), 5.25-5.62(dd, 2H), 4.95(d, 1H), 4.20(m, 1H), 3.64(m, 1H), 3.15(dd, 2H), 1.65(m, 3H), 1.40(m, 3H), 1.15(m, 3H), 0.90(m, 7H), 0.80(t, 3H)

Example 393

N-(1-Naphthylmethyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-8.20(m, 17H), 5.10-5.42(m, 5H), 4.25(m, 1H), 3.40(s, 2H), 3.20(dd, 2H), 1.60(m, 1H), 1.40(m, 1H), 1.05(m, 1H), 0.90(t, 6H)

Example 394

N-(1-Naphthylmethyl)-N-ethoxycarbonylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.10-8.22(m, 13H), 6.30(d, 1H), 5.35(m, 3H), 5.00(d, 2H), 4.25(m, 1H), 4.15(q, 2H), 3.40(s, 2H), 3.05(dd, 2H), 1.60(m, 1H), 1.20-1.40(m, 5H), 0.80(m, 6H)

Example 395

N-(1-Naphthylmethyl)-N-ethylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.05-8.20(m, 13H), 5.55(t, 1H), 5.20-5.40(m, 3H), 4.95(d, 2H), 4.20(m, 1H), 3.60(q, 2H), 3.40(s, 2H), 3.05(dd, 2H), 1.60(m, 1H), 1.40(m, 1H), 1.20(m, 1H), 1.02(t, 3H), 0.85(t, 6H)

Example 396

N-(1-Naphthylmethyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.05-8.20(m, 17H), 5.20-5.40(m, 5H), 4.35(m, 1H), 3.42(s, 2H), 3.20(dd, 2H), 1.65(m, 2H), 1.40(m, 1H), 1.15(m, 1H), 0.90(m, 6H)

Example 397

N-(1-Naphthylmethyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.05-8.20(m, 17H), 5.20-5.40(m, 5H), 4.30(m, 1H), 3.38(s, 2H), 3.20(dd, 2H), 1.60(m, 2H), 1.40(m, 1H), 1.15(m, 1H), 0.90(m, 6H)

Example 398

N-(1-Naphthylmethyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-8.20(m, 17H), 5.20-5.40(m, 5H), 4.25(m, 1H), 3.38(s, 2H), 3.20(dd, 2H), 1.60(m, 2H), 1.40(m, 1H), 1.15(m, 1H), 0.90(m, 6H)

Example 399

N-(1-Naphthylmethyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.80-8.18(m, 17H), 5.20-5.40(m, 5H), 4.23(m, 1H), 3.78(s, 3H), 3.40(s, 2H), 3.20(dd, 2H), 1.60(m, 2H), 1.40(m, 1H), 1.15(m, 1H), 0.90(m, 6H)

Example 400

N-(1-Naphthylmethyl)-N-methylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-8.22(m, 13H), 5.20-5.45(m, 3H), 5.00(d, 2H), 4.20(m, 1H), 3.38(s, 2H), 3.15(dd, 2H), 3.10(d, 3H), 1.60(m, 2H), 1.40(m, 1H), 1.15(m, 1H), 0.90(m, 6H)

Example 401

N-(1-Naphthylmethyl)-N-(1-naphthylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-8.15(m, 20H), 5.20-5.60(m, 5H), 4.40(m, 1H), 3.42(s, 2H), 3.15(dd, 2H), 3.10(d, 3H), 1.60(m, 2H), 1.40(m, 1H), 1.15(m, 1H), 0.90(m, 6H)

Example 402

N-(1-Naphthylmethyl)-N-phenylethylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.75-8.20(m, 18H), 5.20-5.60(m, 3H), 4.80(s, 2H), 4.20(m, 1H), 3.90(m, 1H), 3.70(m, 1H), 3.38(s, 2H), 3.05(dd, 2H), 2.70(t, 2H), 1.60(m, 2H), 1.40(m, 1H), 1.15(m, 1H), 0.90(m, 6H)

Example 403

N-(1-Naphthylmethyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 17H), 5.20-5.60(m, 5H), 4.25(m, 1H), 3.38(s, 2H), 3.20(dd, 2H), 1.60(m, 2H), 1.40(m, 1H), 1.15(m, 1H), 0.90(m, 6H)

Example 404

N-(1-Naphthylmethyl)-N-benzoylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.10-8.20(m, 18H), 6.20(bs, 1H), 5.20-5.55(m, 3H), 5.00(d, 2H), 4.45(m, 1H), 3.50(s, 2H), 3.15(dd, 1H), 1.80(m, 2H), 1.45(m, 1H), 0.85-1.12(m, 7H)

Example 405

N-(1-Naphthylmethyl)-N-cyclohexylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.10-8.20(m, 13H), 5.40(d, 2H), 4.96(d, 2H),

4.20(m, 2H), 3.40(s, 2H), 3.10(dd, 1H), 1.85(bs, 6H), 1.22-1.60(bs, 7H), 0.85-1.12(m, 7H)

Example 406

N-(1-Naphthylmethyl)-N-(4-dimethylamino-1-naphthylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 19H), 5.20-5.55(m, 5H), 4.38(m, 1H), 3.45(s, 2H), 3.25(dd, 1H), 2.80(ss, 6H), 1.80(m, 1H), 1.40(bs, 1H), 1.10(m, 1H), 0.85(m, 6H)

Example 407

N-(1-Naphthylmethyl)-N-(2-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.90-8.18(m, 17H), 6.80(s, 1H), 5.20-5.40(m, 3H), 5.10(d, 2H), 4.35(m, 1H), 3.40(s, 2H), 3.20(dd, 1H), 3.20(s, 3H), 1.80(m, 1H), 1.40(bs, 1H), 1.10(m, 1H), 0.85(m, 6H)

Example 408

N-(1-Naphthylmethyl)-N-(4-nitrophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 17H), 5.60(m, 1H), 5.38(d, 2H), 5.10(d, 2H), 4.25(m, 1H), 3.40(s, 2H), 3.20(dd, 1H), 1.80(m, 1H), 1.40(bs, 1H), 1.10(m, 1H), 0.85(m, 6H)

Example 409

N-(1-Naphthylmethyl)-N-n-propylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine



:

1

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 13H), 5.60(m, 1H), 5.40(d, 2H), 5.25(m, 1H), 4.98(d, 2H), 4.20(m, 1H), 3.60(m, 1H), 3.42(m, 1H), 3.40(s, 2H), 3.10(dd, 1H), 1.80(m, 1H), 1.60(bs, 1H), 1.40(m, 2H), 1.10(m, 1H), 0.85(m, 6H), 0.70(t, 3H)

Example 410

N-(1-Naphthylmethyl)-N-(2-methylphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 17H), 5.25-5.42(m, 3H), 5.10(d, 2H), 4.30(m, 1H), 3.40(s, 2H), 3.22(dd, 1H), 2.00(s, 3H), 1.80(m, 1H), 1.40(m, 1H), 1.10(m, 1H), 0.90(m, 6H)

Example 411

N-(1-Naphthylmethyl)-N-(3-methylphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.96-8.20(m, 17H), 5.40(d, 1H), 5.20(m, 1H), 5.10(d, 2H), 4.25(m, 1H), 3.40(s, 2H), 3.18(dd, 1H), 2.30(s, 3H), 2.00(m, 1H), 1.40(m, 1H), 1.10(m, 1H), 0.90(m, 6H)

Example 412

N-(1-Naphthylmethyl)-N-(4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 17H), 5.40(d, 1H), 5.20(m, 1H), 5.10(d, 2H), 4.30(m, 1H), 3.38(s, 2H), 3.20(dd, 1H), 2.30(s, 3H), 2.00(m, 1H), 1.40(m, 1H), 1.10(m, 1H), 0.90(m, 6H)

Example 413

N-(1-Naphthylmethyl)-N-(4-azidophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.80-8.10(m, 17H), 4.95-5.38(m, 5H), 4.20(m, 1H), 3.27(s, 2H), 3.08(dd, 1H), 1.58(bs, 1H), 1.32(m, 1H), 1.00(m, 1H), 0.92(m, 6H)

Example 414

N-(1-Naphthylmethyl)-N-(4-bromophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.10(m, 17H), 4.92-5.40(m, 5H), 4.20(m, 1H), 3.25(s, 2H), 3.05(dd, 1H), 1.57(bs, 1H), 1.34(m, 1H), 0.98(m, 1H), 0.82(m, 6H)

Example 415

N-(1-Naphthylmethyl)-N-(2-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.15(m, 17H), 5.00-5.38(m, 5H), 4.24(m, 1H), 3.32(s, 2H), 3.13(dd, 1H), 1.58(bs, 1H), 1.36(m, 1H), 1.00(m, 1H), 0.80(m, 6H)

Example 416

N-(1-Naphthylmethyl)-N-(3-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.10(m, 17H), 4.98-5.22(m, 5H), 4.20(m, 1H), 3.28(s, 2H), 3.10(dd, 1H), 1.56(bs, 1H), 1.35(m, 1H), 1.00(m, 1H),

0.80(m, 6H)

Example 417

N-(1-Naphthylmethyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-8.15(m, 16H), 5.00-5.18(m, 5H), 4.25(m, 1H), 3.30(s, 2H), 3.14(dd, 1H), 1.60(bs, 1H), 1.34(m, 1H), 1.00(m, 1H), 0.82(m, 6H)

Example 418

N-(1-Naphthylmethyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

<Step 1>

N-(1-Naphthylmethyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

Using the same method as described in Preparative Example 3 N-*t*-butoxycarbonyl-L-isoleucine was converted to N-(*t*-butoxycarbonyl)-L-isoleucine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride with 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride to give the title compound.

¹H-NMR (CDCl₃) : δ 6.80-8.20(m, 13H), 5.95(d, 1H), 4.80-5.12(dd, 2H), 4.15-4.20(m, 2H), 3.80-4.00(m, 1H), 3.15(m, 2H), 2.60-2.80(m, 2H), 2.24(bs, 1H), 1.20-1.60(m, 2H), 0.92-1.20(m, 1H), 0.60-0.92(m, 6H)

<Step 2>

N-(1-Naphthylmethyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of N-(1-naphthylmethyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added 2-bromophenylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 4hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: CH₂Cl₂/MeOH=9/1, v/v) to give the title compound as a white solid.

¹H-NMR (CDCl₃) : δ 7.10-8.00(m, 17H), 5.40(m, 2H), 5.20(d, 4H), 4.40(m, 2H), 4.05(bs, 1H), 3.40(s, 2H), 3.25(dd, 1H), 1.80(m, 1H), 1.42(bs, 1H), 0.80-1.10(m, 7H)

Examples 419-447

N-(1-Naphthylmethyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 418 to give the title compounds.

Example 419

N-(1-Naphthylmethyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.10-8.00(m, 17H), 5.00-5.40(m, 4H), 4.25(m, 1H), 4.05(bs, 1H), 3.36(s, 2H), 3.20(dd, 1H), 1.80(m, 1H), 1.42(bs, 1H), 0.80-1.10(m, 7H)

Example 420

N-(1-Naphthylmethyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-7.95(m, 17H), 5.05-5.40(m, 4H), 4.35(m, 1H), 4.10(bs, 1H), 3.40(s, 2H), 3.20(dd, 1H), 1.80(m, 1H), 1.42(bs, 1H), 0.80-1.10(m, 7H)

Example 421

N-(1-Naphthylmethyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.90-7.95(m, 17H), 5.05-5.50(m, 5H), 4.25(m, 1H), 3.38(s, 2H), 3.18(dd, 1H), 1.60(m, 1H), 1.40(bs, 1H), 1.05(m, 1H), 0.80(t, 6H)

Example 422

N-(1-Naphthylmethyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.95(m, 17H), 5.30(d, 2H), 5.20-5.42(m, 1H), 5.15(m, 2H), 4.20(m, 1H), 3.40(s, 2H), 3.20(dd, 1H), 1.80(m, 1H), 1.40(m, 1H), 1.04(m, 1H), 0.85(t, 6H)

Example 423

N-(1-Naphthylmethyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.80-7.95(m, 17H), 5.25-5.40(m, 3H), 5.10(m,

2H), 4.25(m, 1H), 3.75(s, 3H), 3.40(s, 2H), 3.20(dd, 1H), 1.80(m, 1H), 1.40(m, 1H), 1.04(m, 1H), 0.85(m, 6H)

Example 424

N-(1-Naphthylmethyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.90(m, 17H), 5.05-5.50(m, 5H), 4.30(m, 1H), 3.35(s, 2H), 3.20(dd, 1H), 1.80(m, 1H), 1.40(m, 1H), 1.04(m, 1H), 0.85(m, 6H)

Example 425

N-(1-Naphthylmethyl)-N-(2-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.88-8.20(m, 17H), 4.85-5.35(m, 5H), 4.30(m, 1H), 3.40(s, 2H), 3.22(s, 3H), 3.20(dd, 1H), 1.75(m, 1H), 1.40(m, 1H), 1.05(m, 1H), 0.90(m, 6H)

Example 426

N-(1-Naphthylmethyl)-N-(4-nitrophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-8.15(m, 17H), 5.55(m, 1H), 5.30(d, 2H), 5.05(d, 2H), 4.24(m, 1H), 3.38(s, 2H), 3.20(dd, 1H), 1.75(m, 1H), 1.40(m, 1H), 1.05(m, 1H), 0.90(m, 6H)

Example 427

N-(1-Naphthylmethyl)-N-(2-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-8.20(m, 17H), 5.30(m, 3H), 5.10(dd, 2H), 3.40(s, 2H), 3.20(dd, 1H), 1.98(s, 3H), 1.60(m, 1H), 1.40(m, 1H), 1.10(m, 1H), 0.95(m, 6H)

Example 428

N-(1-Naphthylmethyl)-N-(3-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.90-7.90(m, 17H), 5.35(m, 3H), 5.10(d, 2H), 3.38(s, 2H), 3.20(dd, 1H), 2.25(s, 3H), 1.60(m, 1H), 1.40(m, 1H), 1.10(m, 1H), 0.95(m, 6H)

Example 429

N-(1-Naphthylmethyl)-N-(4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-7.95(m, 17H), 5.30(m, 3H), 5.10(dd, 2H), 3.40(s, 2H), 3.18(dd, 1H), 2.30(s, 3H), 1.55(m, 1H), 1.42(m, 1H), 1.05(m, 1H), 0.85(m, 6H)

Example 430

N-(1-Naphthylmethyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-7.95(m, 13H), 5.60(t, 1H), 5.35(m, 3H), 4.98(d, 2H), 4.20(m, 1H), 3.65(m, 1H), 3.42(m, 1H), 3.38(s, 2H), 3.10(dd, 1H), 1.65(m, 1H), 1.40(m, 1H), 1.10(m, 1H), 0.85(m, 6H)

Example 431

N-(1-Naphthylmethyl)-N-benzylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-7.90(m, 18H), 6.00(t, 1H), 5.30(s, 2H), 5.20(m, 1H), 5.05(dd, 2H), 4.80(d, 2H), 4.24(m, 1H), 3.28(s, 2H), 3.15(dd, 1H), 1.58(m, 1H), 1.40(m, 1H), 1.05(m, 1H), 0.85(t, 6H)

Example 432

N-(1-Naphthylmethyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.10-7.95(m, 17H), 5.60(m, 1H), 5.30(s, 2H), 5.10(m, 2H), 4.30(m, 1H), 3.38(s, 2H), 3.20(dd, 1H), 1.60(m, 1H), 1.40(m, 1H), 1.05(m, 1H), 0.85(t, 6H)

Example 433

N-(1-Naphthylmethyl)-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-7.95(m, 13H), 5.70(m, 3H), 5.38(m, 2H), 4.95(m, 2H), 4.20(m, 3H), 3.35(s, 2H), 3.10(dd, 1H), 1.60(m, 1H), 1.42-1.55(m, 3H), 1.05-2.22(m, 3H), 0.85(m, 9H)

Example 434

N-(1-Naphthylmethyl)-N-ethylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-7.95(m, 13H), 5.62(m, 1H), 5.35(m, 2H), 5.00(m, 2H), 4.20(m, 1H), 3.60(m, 2H), 3.35(s, 2H), 3.10(dd, 1H), 1.60(m, 1H), 1.40(m, 1H), 1.10(m, 1H), 1.04(t, 3H), 0.85(m, 6H)

Example 435

N-(1-Naphthylmethyl)-N-(4-azidophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.95-7.95(m, 17H), 5.04-5.42(m, 5H), 4.25(m, 1H), 3.36(s, 2H), 3.18(dd, 1H), 1.60(m, 1H), 1.40(m, 1H), 1.08(m, 1H), 0.85(t, 6H)

Example 436

N-(1-Naphthylmethyl)-N-(4-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.02-7.90(m, 17H), 5.04-5.48(m, 5H), 4.28(m, 1H), 3.38(s, 2H), 3.20(tt, 1H), 1.60(m, 1H), 1.40(m, 1H), 1.05(m, 1H), 0.86(t, 6H)

Example 437

N-(1-Naphthylmethyl)-N-(2-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.05-7.90(m, 17H), 5.08-5.46(m, 5H), 4.40(m, 1H), 3.40(s, 2H), 3.22(tt, 1H), 1.62(m, 1H), 1.41(m, 1H), 1.07(m, 1H), 0.85(m, 6H)

Example 438

N-(1-Naphthylmethyl)-N-methylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-7.95(m, 13H), 5.78(m, 1H), 5.20-5.40(m,

2H), 5.00(m, 2H), 4.20(m, 1H), 3.60(m, 2H), 3.34(s, 2H), 3.10(dd, 1H), 3.00(d, 3H), 1.60(m, 1H), 1.40(m, 1H), 1.10(m, 1H), 0.85(m, 6H)

Example 439

N-(1-Naphthylmethyl)-N-(1-naphthylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-8.00(m, 20H), 5.55(dd, 1H), 5.25(d, 2H), 5.20(d, 2H), 4.40(m, 1H), 3.40(s, 2H), 3.25(dd, 1H), 3.00(d, 3H), 1.60(m, 1H), 1.40(m, 1H), 1.10(m, 1H), 0.85(t, 6H)

Example 440

N-(1-Naphthylmethyl)-N-phenylethylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.80-7.95(m, 18H), 5.50(m, 1H), 5.35(d, 2H), 4.80(d, 2H), 4.20(m, 1H), 3.90(m, 1H), 3.70(m, 1H), 3.35(s, 2H), 3.05(dd, 3H), 2.70(m, 2H), 1.40(m, 1H), 1.10(m, 1H), 0.85(t, 6H)

Example 441

N-(1-Naphthylmethyl)-N-benzoylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-7.90(m, 18H), 6.20(m, 1H), 5.40(d, 2H), 5.00(dd, 2H), 4.40(m, 1H), 3.52(d, 2H), 3.05(m, 3H), 1.60(m, 1H), 1.40(m, 1H), 1.10(m, 1H), 0.80(m, 6H)

Example 442

N-(1-Naphthylmethyl)-N-cyclohexylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.20-7.98(m, 13H), 5.22-5.40(m, 3H), 5.00(m, 2H), 4.22(m, 2H), 3.35(s, 2H), 3.05(dd, 3H), 1.92(bs, 4H), 1.30-1.62(m, 6H), 1.10(m, 3H), 0.90(m, 6H)

Example 443

N-(1-Naphthylmethyl)-N-(4-dimethylamino-1-naphthylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 19H), 5.20-5.60(m, 5H), 4.42(m, 1H), 3.40(s, 2H), 3.25(dd, 1H), 2.85(s, 6H), 1.60(m, 1H), 1.40(m, 1H), 1.05(m, 1H), 0.84(t, 6H)

Example 444

N-(1-Naphthylmethyl)-N-phenylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.05-7.95(m, 18H), 5.22-5.44(m, 3H), 5.10(dd, 2H), 4.30(m, 1H), 3.38(s, 2H), 3.18(dd, 1H), 1.60(m, 1H), 1.40(m, 1H), 1.10(m, 1H), 0.85(t, 6H)

Example 445

N-(1-Naphthylmethyl)-N-(n-propylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.05-7.95(m, 13H), 5.60(t, 1H), 5.20-5.38(m, 3H), 4.98(d, 2H), 4.25(m, 1H), 3.60(m, 1H), 3.42(m, 1H), 3.38(s, 2H), 3.10(tt, 1H), 1.60(m, 1H), 1.42(q, 2H), 1.40(m, 1H), 1.10(m, 1H), 0.85(t, 6H), 0.70(t, 3H)

Example 446

N-(1-Naphthylmethyl)-N-(3-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-7.92(m, 17H), 5.00-5.55(m, 5H), 4.32(m, 1H), 3.38(s, 2H), 3.18(tt, 1H), 1.60(m, 1H), 1.40(m, 1H), 1.08(m, 1H), 0.88(m, 6H)

Example 447

N-(1-Naphthylmethyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.05-7.90(m, 16H), 5.05-5.45(m, 5H), 4.38(m, 1H), 3.38(s, 2H), 3.20(tt, 1H), 1.65(m, 1H), 1.42(m, 1H), 1.08(m, 1H), 0.86(t, 6H)

Example 448

N-(1-Naphthylmethyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

<Step 1>

N-(1-Naphthylmethyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

Using the same method as described in Preparative Example 3, N-*t*-butoxycarbonyl-L-valine was converted to N-(*t*-butoxycarbonyl)-L-valine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4 to give the title compound.

TLC : $R_f = 0.31$ (CH_2Cl_2 / $\text{MeOH} = 10 / 1$)

$^1\text{H-NMR}$ (CDCl_3) : δ 8.00-8.20(m, 3H), 7.70-7.95(m, 2H), 7.23-7.60(m, 5H), 6.90-7.06(m, 3H), 5.80(d, 1H), 5.10(d, 1H), 4.20(s, 2H), 3.70-3.90(m, 1H), 3.00-3.30(dd, 2H), 2.85-3.00(m, 1H), 2.65-2.83(m, 2H), 2.00(b, 1H), 1.60-1.80(m, 1H), 0.75-1.00(m, 6H)

<Step 2>

N-(1-Naphthylmethyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

To a solution of N-(1-naphthylmethyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added allylisothiocyanate (0.1M in CH_2Cl_2 , 0.2ml, 0.02mmol). The reaction mixture was agitated for 4hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: $\text{CH}_2\text{Cl}_2/\text{MeOH}=9/1$, v/v) to give the title compound as a white solid.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.05-8.20(m, 13H), 5.70(m, 2H), 5.40(d, 2H), 5.20(m, 1H), 4.22(m, 3H), 3.38(s, 2H), 3.10(dd, 1H), 1.80(m, 1H), 0.90(d, 6H)

Examples 449-463

N-(1-Naphthylmethyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 448 to give the title compounds.

Example 449

N-(1-Naphthylmethyl)-N-benzylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 7.05-8.20(m, 18H), 6.00(t, 1H), 5.20-5.38(m, 3H), 5.05(d, 2H), 4.82(d, 2H), 4.18(m, 1H), 3.35(s, 2H), 3.17(dd, 1H), 1.80(m, 1H), 0.85(d, 6H)

Example 450

N-(1-Naphthylmethyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 7.10-8.20(m, 17H), 5.05-5.45(m, 5H), 4.30(m, 1H), 3.42(s, 2H), 3.20(dd, 1H), 1.82(m, 1H), 0.90(dd, 6H)

Example 451

N-(1-Naphthylmethyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 7.10-8.20(m, 17H), 5.25-5.42(m, 3H), 5.15(m, 2H), 4.20(m, 1H), 3.40(s, 2H), 3.20(dd, 1H), 1.85(m, 1H), 0.90(dd, 6H)

Example 452

N-(1-Naphthylmethyl)-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 7.05-8.20(m, 13H), 5.45(d, 2H), 5.22(m, 1H), 4.96(d, 2H), 4.18(m, 1H), 3.65(m, 1H), 3.42(s, 2H), 3.40(s, 2H), 3.15(dd, 1H), 1.80(m, 1H), 1.38(q, 2H), 1.10(q, 2H), 0.90(dd, 6H), 0.78(t, 3H)

Example 453

N-(1-Naphthylmethyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3) : \delta$ 7.05-8.20(m, 17H), 5.22-5.45(m, 3H), 5.10(d, 2H), 4.20(m, 1H), 3.65(m, 1H), 3.38(s, 2H), 1.82(m, 1H), 0.85(dd, 6H)

Example 454

N-(1-Naphthylmethyl)-N-ethoxycarbonylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3) : \delta$ 7.10-8.22(m, 13H), 6.20(d, 1H), 5.18-5.45(m, 3H), 4.95(d, 1H), 4.22(m, 1H), 4.15(q, 2H), 3.70(s, 2H), 3.42(s, 2H), 3.08(dd, 1H), 1.65(m, 1H), 1.22(t, 2H), 0.75(t, 6H)

Example 455

N-(1-Naphthylmethyl)-N-ethylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3) : \delta$ 7.05-7.95(m, 13H), 5.43(d, 2H), 5.20(m, 1H), 4.97(d, 2H), 4.15(m, 1H), 3.60(m, 2H), 3.40(s, 2H), 3.10(dd, 1H), 1.78(m, 1H), 1.00(t, 2H), 0.87(t, 6H)

Example 456

N-(1-Naphthylmethyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3) : \delta$ 6.98-8.18(m, 17H), 5.05-5.42(m, 5H), 4.25(m, 1H), 3.43(s, 2H), 3.20(dd, 1H), 1.80(m, 1H), 0.90(t, 6H)

Example 457

N-(1-Naphthylmethyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 6.85-8.18(m, 17H), 5.05-5.45(m, 5H), 4.20(m, 1H), 3.40(s, 2H), 3.20(dd, 1H), 1.85(m, 1H), 0.90(d, 6H)

Example 458

N-(1-Naphthylmethyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 6.90-8.20(m, 17H), 5.20-5.42(m, 3H), 5.05(d, 2H), 4.20(m, 1H), 3.38(s, 2H), 3.20(dd, 1H), 1.82(m, 1H), 0.87(m, 6H)

Example 459

N-(1-Naphthylmethyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 6.80-8.20(m, 17H), 5.20-5.45(m, 3H), 5.05(d, 2H), 4.22(m, 1H), 3.78(s, 3H), 3.40(s, 2H), 3.20(dd, 1H), 1.82(m, 1H), 0.87(d, 6H)

Example 460

N-(1-Naphthylmethyl)-N-methylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 7.05-8.22(m, 13H), 5.15-5.45(m, 3H), 4.98(d, 2H), 4.18(m, 1H), 3.44(s, 2H), 3.15(dd, 1H), 3.08(s, d), 1.82(m, 1H), 0.87(d, 6H)

Example 461

N-(1-Naphthylmethyl)-N-(1-naphthylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 7.04-8.15(m, 20H), 5.18-5.60(m, 5H), 4.30(m, 1H), 3.40(s, 2H), 3.22(dd, 1H), 1.80(m, 1H), 0.85(m, 6H)

Example 462

N-(1-Naphthylmethyl)-N-phenylethylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 6.78-8.20(m, 18H), 5.45(m, 1H), 5.40(d, 2H), 5.25(dd, 2H), 4.10(m, 1H), 3.92(m, 1H), 3.70(m, 1H), 3.38(s, 2H), 3.10(dd, 1H), 2.72(m, 2H), 1.80(m, 1H), 0.90(d, 6H)

Example 463

N-(1-Naphthylmethyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 6.92-8.18(m, 17H), 5.55(d, 1H), 5.30(d, 2H), 5.15(m, 2H), 4.22(m, 1H), 3.40(s, 2H), 3.20(dd, 1H), 1.84(m, 1H), 0.95(t, 6H)

Example 464

N-(1-Naphthylmethyl)-N-(3-bromophenylthiocarbamoyl)-2-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

<Step 1>

N-(1-Naphthylmethyl)-2-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

Using the same method as described in Preparative Example 3, N-*t*-butoxycarbonyl-L-glycine was converted to N-(*t*-butoxycarbonyl)-L-glycine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4 to give the title compound.

TLC : $R_f = 0.15$ (CH_2Cl_2 / MeOH = 5 / 1)

$^1\text{H-NMR}$ (CDCl_3) : δ 8.10(d, 3H), 7.65-7.95(m, 2H), 7.40-7.43(m, 5H), 7.08(d, 2H), 6.95(s, 1H), 6.23(b, 1H), 5.18(s, 2H), 4.23(s, 2H), 3.20-3.30(m, 4H), 2.80(t, 2H), 1.97-2.20(b, 1H)

<Step 2>

N-(1-Naphthylmethyl)-N-(3-bromophenylthiocarbamoyl)-2- $\{[1-(4\text{-nitrobenzyl})\text{-}1\text{H-imidazol-5-yl]acetyl}\}$ aminoethylamine

To a solution of N-(1-naphthylmethyl)-2- $\{[1-(4\text{-nitrobenzyl})\text{-}1\text{H-imidazol-5-yl]acetyl}\}$ aminoethylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added 3-bromophenylisothiocyanate (0.1M in CH_2Cl_2 , 0.2ml, 0.02mmol). The reaction mixture was agitated for 3hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: $\text{CH}_2\text{Cl}_2/\text{MeOH}=9/1$, v/v) to give the title compound as a white solid.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 17H), 6.48(bs, 1H), 5.50(s, 2H), 5.25(s, 2H), 3.80(t, 2H), 3.32(s, 2H), 3.00(t, 2H)

Examples 465-469

N-(1-Naphthylmethyl)-2(S)- $\{[1-(4\text{-nitrobenzyl})\text{-}1\text{H-imidazol-5-yl]acetyl}\}$ aminoethylamine was reacted with the corresponding

isothiocyanates under the same condition as described in <Step 2> of Example 464 to give the title compounds.

Example 465

N-(1-Naphthylmethyl)-N-(4-chlorophenylthiocarbamoyl)-2- {[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR (CDCl₃) : δ 7.00-8.18(m, 17H), 6.60(bs, 1H), 5.45(s, 2H), 5.23(s, 2H), 3.82(t, 2H), 3.35(s, 2H), 3.02(t, 2H)

Example 466

N-(1-Naphthylmethyl)-N-(3-fluorophenylthiocarbamoyl)-2- {[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR (CDCl₃) : δ 6.85-8.40(m, 17H), 6.58(bs, 1H), 5.48(s, 2H), 5.25(s, 2H), 3.80(t, 2H), 3.35(s, 2H), 3.02(t, 2H)

Example 467

N-(1-Naphthylmethyl)-N-(4-fluorophenylthiocarbamoyl)-2- {[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR (CDCl₃) : δ 7.00-8.15(m, 17H), 6.64(bs, 1H), 5.42(s, 2H), 5.24(s, 2H), 3.85(t, 2H), 3.34(s, 2H), 3.10(t, 2H)

Example 468

N-(1-Naphthylmethyl)-N-(4-methoxyphenylthiocarbamoyl)-2- {[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR (CDCl₃) : δ 6.85-8.18(m, 17H), 5.40(s, 2H), 5.28(s, 2H), 4.00(t, 2H), 3.78(s, 3H), 3.38(s, 2H), 3.12(t, 2H)

Example 469

N-(1-Naphthylmethyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

¹H-NMR (CDCl₃) : δ 6.92-8.15(m, 17H), 6.42(bs, 1H), 5.55(s, 2H), 5.28(s, 2H), 3.75(s, 2H), 2.98(t, 2H)

Example 470

N-(1-Naphthylmethyl)-N-(3-bromophenylthiocarbamoyl)-2-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

<Step 1>

2-(*t*-Butoxycarbonyl)amino-2-methylpropionic acid

To a solution of 2-amino-2-methylpropionic acid (15.0 g, 146 mmol) in dioxane (290 ml) and water (145 ml) was added 1N NaOH (146 ml) and then di-*t*-butyl pyrocarbonate (36.8 ml, 160 mmol) was added dropwise thereto at 0°C. The reaction mixture was stirred at room temperature for 30 min. The solution was concentrated *in vacuo* to the volume of about 200ml and cooled in an ice-water bath. After addition of ethyl acetate (300 ml), the mixture was acidified with an aqueous solution of potassium bisulfate to pH=2~3. The organic layer was washed with water, saturated sodium bicarbonate solution and brine, dried over MgSO₄ and concentrated *in vacuo* to give the title compound (25.1 g, 85 %) as a white solid.

¹H-NMR (CDCl₃) : δ 9.40-10.60(bs, 1H), 5.00-5.40(bs, 1H), 1.58(s, 6H), 1.43(s, 9H)

<Step 2>

2-(*t*-Butoxycarbonyl)amino-2-methylpropanol

To a solution of 2-(*t*-butoxycarbonyl)amino-2-methylpropionic acid (9.54 g, 47 mmol) in dry tetrahydrofuran (250ml) was added triethylamine (6.54 ml 47 mmol), and then ethylchloroformate (5.38 ml, 564 mmol) was added dropwise thereto while maintaining the temperature at 5°C. The reaction mixture was stirred at 5°C for 30min. The precipitate was filtered off. To the filtrate was added dropwise sodium borohydride (3.55 g, 94.0 mmol) in water (50 ml) at 0°C. The reaction mixture was stirred for 1hr at room temperature and concentrated *in vacuo*. The residue was partitioned between 2N HCl (100 ml) and ethyl acetate (150 ml). The organic layer was washed with water, saturated sodium bicarbonate solution and brine, dried over MgSO₄ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography(eluent: EtOAc/n-hexane=1/2, v/v) to give the title compound (7.10 g, 80 %) as a white solid.

TLC : R_f=0.38 (EtOAc / n-hexane = 1 / 2)

¹H-NMR (CDCl₃) : δ 4.60-4.80(b, 1H), 3.58(s, 2H), 1.43(s, 9H), 1.25(s, 6H)

<Step 3>

2-(*t*-Butoxycarbonyl)amino-2-methylpropione aldehyde

To a solution of oxalylchloride (4.39 ml, 50.3 mmol) in dichloromethane (90ml) was added a solution of dimethylsulfoxide (7.14 ml, 101 mmol) in dichloromethane (20 ml) dropwise for 5min at -60°C ~ -70°C. The reaction mixture was stirred for 30min. To the above solution was added a solution of 2-(*t*-butoxycarbonyl)amino-2-methyl-

propanol (8.65 g, 457 mmol) in dichloromethane (40 ml) dropwise. The reaction mixture was stirred for 1hr while maintaining the temperature at -60°C. To the reaction mixture was added triethylamine (31.9 ml, 229 mmol) dropwise. The mixture was stirred for 1hr at room temperature. After the addition of dichloromethane (100 ml), the reaction mixture was washed with 5% HCl and saturated sodium bicarbonate solution, dried over MgSO₄ and concentrated *in vacuo*. The residue was purified by silica gel column chromatography(eluent: EtOAc/n-hexane=1/2, v/v) to give the title compound (7.96 g, 93 %) as a white solid.

¹H-NMR (CDCl₃) : δ 9.44(s, 1H), 5.03(b, 1H), 1.44(s, 9H), 1.33(s, 6H)

<Step 4>

N-(1-Naphthylmethyl)-2-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

The reaction was carried out under the same condition as described in Preparative Example 4, but replacing N-(t-butoxycarbonyl)-L-isoleucine aldehyde and 2,3-dichlorobenzylamine with 2-(t-butoxycarbonyl)amino-2-methylpropion aldehyde and 1-naphthylmethylamine, respectively, to give the title compound.

TLC : R_f = 0.31 (CH₂Cl₂ / MeOH = 9 / 1)

¹H-NMR (CDCl₃) : δ 7.92-8.20(dd, 3H), 7.62-7.90(m, 2H), 7.25-7.60(m, 5H), 7.03(d, 2H), 6.82(s, 1H), 6.23(s, 1H), 5.20(s, 2H), 4.20(s, 2H), 3.02(s, 2H), 2.62(s, 2H), 2.18(b, 1H), 1.23(s, 6H)

<Step 5>

N-(1-Naphthylmethyl)-N-(3-bromophenylthiocarbamoyl)-2-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

To a solution of N-(1-naphthylmethyl)-2-{{1-(4-nitrobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added 3-bromophenylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 4hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: CH₂Cl₂/MeOH=9/1, v/v) to give the title compound as a white solid.

¹H-NMR (CDCl₃) : δ 7.00-8.20(m, 17H), 5.45(s, 2H), 5.34(s, 2H), 4.14(s, 2H), 3.22(s, 2H), 1.45(s, 6H)

Examples 471-475

N-(1-Naphthylmethyl)-2-{{1-(4-nitrobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 5> of Example 470 to give the title compounds.

Example 471

N-(1-Naphthylmethyl)-N-(4-chlorophenylthiocarbamoyl)-2-{{1-(4-nitrobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

¹H-NMR (CDCl₃) : δ 7.00-8.18(m, 17H), 5.48(s, 2H), 5.32(s, 2H), 4.15(s, 2H), 3.22(s, 2H), 1.45(s, 6H)

Example 472

N-(1-Naphthylmethyl)-N-(2-fluorophenylthiocarbamoyl)-2-{{1-(4-nitrobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 17H), 5.45(s, 2H), 5.35(s, 2H), 4.20(s, 2H), 3.22(s, 2H), 1.48(s, 6H)

Example 473

N-(1-Naphthylmethyl)-N-(3-fluorophenylthiocarbamoyl)-2- $\{[1-(4\text{-nitrobenzyl})$ -1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.90-8.20(m, 17H), 5.50(s, 2H), 5.35(s, 2H), 4.18(s, 2H), 3.22(s, 2H), 1.48(s, 6H)

Example 474

N-(1-Naphthylmethyl)-N-(4-fluorophenylthiocarbamoyl)-2- $\{[1-(4\text{-nitrobenzyl})$ -1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 17H), 5.48(s, 2H), 5.38(s, 2H), 4.20(s, 2H), 3.22(s, 2H), 1.52(s, 6H)

Example 475

N-(1-Naphthylmethyl)-N-(4-methoxyphenylthiocarbamoyl)-2- $\{[1-(4\text{-nitrobenzyl})$ -1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.80-8.20(m, 17H), 5.42(s, 2H), 5.40(s, 2H), 4.20(bs, 2H), 3.78(s, 3H), 3.22(s, 2H), 1.50(s, 6H)

Example 476

N-(1-Naphthylmethyl)-N-benzylthiocarbamoyl-2(S)- $\{[1-(4\text{-nitrobenzyl})$ -1H-imidazol-5-yl]acetyl}aminopentylamine

<Step 1>

N-(1-Naphthylmethyl)-2(S)- $\{[1-(4\text{-nitrobenzyl})$ -1H-imidazol-5-yl]acetyl}amin

opentylamine

Using the same method as described in Preparative Example 3, N-*t*-butoxycarbonyl-L-norvaline was converted to N-*t*-butoxycarbonyl-L-norvaline aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4 to give the title compound.

TLC : $R_f = 0.39$ (CH_2Cl_2 / MeOH = 10 / 1)

$^1\text{H-NMR}$ (CDCl_3) : δ 8.14(m, 3H), 7.70-8.00(m, 2H), 7.37-7.62(m, 5H), 7.03(d, 2H), 6.92(s, 1H), 5.81(d, 1H), 5.10(dd, 2H), 4.20(s, 2H), 3.90-4.10(m, 1H), 3.17(dd, 2H), 2.72(m, 2H), 1.82(s, 1H), 1.30-1.50(m, 4H), 0.80-1.00(m, 3H)

<Step 2>

N-(1-Naphthylmethyl)-N-benzylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminopentylamine

To a solution of N-(1-naphthylmethyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminopentylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added benzylisothiocyanate (0.1M in CH_2Cl_2 , 0.2ml, 0.02mmol). The reaction mixture was agitated for 4hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: $\text{CH}_2\text{Cl}_2/\text{MeOH}=9/1$, v/v) to give the title compound as a white solid.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 18H), 5.35(d, 2H), 5.20(m, 1H), 5.02(m, 2H), 4.82(d, 2H), 4.24(m, 1H), 3.25(s, 2H), 3.12(dd, 1H), 1.40(m, 4H), 0.85 (t, 3H)

Example 477-487

N-(1-Naphthylmethyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminopentylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 476 to give the title compounds.

Example 477

N-(1-Naphthylmethyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminopentylamine

¹H-NMR (CDCl₃) : δ 7.05-8.18(m, 17H), 5.50(d, 2H), 5.35(s, 2H), 5.18(m, 2H), 4.40(m, 1H), 3.40(s, 2H), 3.22(dd, 1H), 1.44(m, 4H), 0.85(t, 3H)

Example 478

N-(1-Naphthylmethyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminopentylamine

¹H-NMR (CDCl₃) : δ 7.05-8.20(m, 17H), 5.60(d, 1H), 5.32(s, 2H), 5.08(d, 1H), 4.82 (bs, 1H), 4.25(m, 1H), 3.38(s, 2H), 3.16(dd, 1H), 1.42(m, 4H), 0.85 (t, 3H)

Example 479

N-(1-Naphthylmethyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminopentylamine

¹H-NMR (CDCl₃) : δ 7.05-8.20(m, 17H), 5.34(d, 2H), 5.05-5.60(dd, 2H), 4.90 (bs, 1H), 4.25(m, 1H), 3.38(s, 2H), 3.20(dd, 1H), 1.40(m, 4H), 0.84 (t, 3H)

Example 480

N-(1-Naphthylmethyl)-N-ethylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminopentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.05-8.20(m, 13H), 5.40(d, 2H), 4.90-5.30(m, 3H), 4.20(m, 1H), 3.58(m, 2H), 3.35(s, 2H), 3.05(dd, 1H), 1.40(m, 4H), 1.05 (t, 3H), 0.84 (t, 3H)

Example 481

N-(1-Naphthylmethyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminopentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.18(m, 17H), 5.32(s, 2H), 5.00-5.52(m, 3H), 4.35 (bs, 1H), 3.40(s, 2H), 3.20(dd, 1H), 1.42(m, 4H), 0.86 (t, 3H)

Example 482

N-(1-Naphthylmethyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminopentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.85-8.20(m, 17H), 5.58(d, 2H), 5.35(s, 2H), 5.10(d, 1H), 4.90 (bs, 1H), 4.25(m, 1H), 3.38(s, 2H), 3.18(dd, 1H), 1.42(m, 4H), 0.85 (t, 3H)

Example 483

N-(1-Naphthylmethyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminopentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.98-8.20(m, 17H), 5.35(s, 2H), 5.02-5.58(m, 2H), 4.95 (bs, 1H), 4.25 (bs, 1H), 3.35(s, 2H), 3.20(dd, 1H), 1.42(m, 4H),

0.85 (t, 3H)

Example 484

N-(1-Naphthylmethyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminopentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.80-8.20(m, 17H), 5.45(m, 1H), 5.38(d, 2H), 5.10(d, 2H), 4.30 (bs, 1H), 3.38(s, 2H), 3.18(dd, 1H), 1.40(m, 4H), 0.85 (t, 3H)

Example 485

N-(1-Naphthylmethyl)-N-methylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminopentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 13H), 5.40(d, 2H), 4.90-5.30(m, 3H), 4.20 (bs, 1H), 3.35(s, 2H), 3.10(dd, 1H), 3.07(d, 3H), 1.40(m, 4H), 0.85 (t, 3H)

Example 486

N-(1-Naphthylmethyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminopentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.02-8.18(m, 17H), 5.72(d, 1H), 5.30(s, 2H), 5.10(d, 1H), 4.75 (bs, 1H), 4.22 (bs, 1H), 3.38(s, 2H), 3.16(dd, 1H), 1.30-1.50(m, 4H), 0.88 (t, 3H)

Example 487

N-(1-Naphthylmethyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}aminopentylamine

¹H-NMR (CDCl₃) : δ 7.02-8.20(m, 13H), 5.78(m, 1H), 5.40(d, 2H), 4.90-5.30(m, 5H), 4.22(m, 3H), 3.35(s, 2H), 3.10(dd, 1H), 1.30-1.50(m, 4H), 0.88 (t, 3H)

Example 488

N-(1-Naphthylmethyl)-N-(2-bromophenylthiocarbamoyl)-2-{{1-(4-nitrobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-cyclohexylethylamine

<Step 1>

N-(1-Naphthylmethyl)-2-{{1-(4-nitrobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-cyclohexylethylamine

Using the same method as described in Preparative Example 3, N-*t*-butoxycarbonyl-2-amino-2-cyclohexylacetic acid was converted to N-(*t*-butoxycarbonyl)-2-amino-2-cyclohexylacetaldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4 to give the title compound.

<Step 2>

N-(1-Naphthylmethyl)-N-(2-bromophenylthiocarbamoyl)-2-{{1-(4-nitrobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-cyclohexylethylamine

To a solution of N-(1-naphthylmethyl)-2-{{1-(4-nitrobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-cyclohexylethylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added 2-bromophenylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 4hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: CH₂Cl₂/MeOH=9/1, v/v) to give the title compound as a white solid.

$^1\text{H-NMR}$ (CDCl_3) : δ 6.95-8.15(m, 17H), 5.54(s, 2H), 5.22(s, 2H), 4.26 (bs, 2H), 3.15(s, 2H), 2.40 (bs, 2H), 1.20-1.75 (bs, 8H)

Examples 489-491

N-(1-Naphthylmethyl)-2- $\{[1-(4\text{-nitrobenzyl})\text{-}1\text{H-imidazol-}5\text{-yl]acetyl}\}$ amino-2-cyclohexylethylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 488 to give the title compounds.

Example 489

N-(1-Naphthylmethyl)-N-(4-fluorophenylthiocarbamoyl)-2- $\{[1-(4\text{-nitrobenzyl})\text{-}1\text{H-imidazol-}5\text{-yl]acetyl}\}$ amino-2-cyclohexylethylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.95-8.18(m, 17H), 5.60 (bs, 2H), 5.20(s, 2H), 4.12 (bs, 2H), 3.18(s, 2H), 2.28 (bs, 2H), 1.20-1.75 (bs, 8H)

Example 490

N-(1-Naphthylmethyl)-N-(4-methoxyphenylthiocarbamoyl)-2- $\{[1-(4\text{-nitrobenzyl})\text{-}1\text{H-imidazol-}5\text{-yl]acetyl}\}$ amino-2-cyclohexylethylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.80-8.15(m, 17H), 5.58 (bs, 2H), 5.20(s, 2H), 4.18 (bs, 2H), 3.18(s, 2H), 2.32 (bs, 2H), 1.40-1.85 (bs, 8H)

Example 491

N-(1-Naphthylmethyl)-N-methylthiocarbamoyl-2- $\{[1-(4\text{-nitrobenzyl})\text{-}1\text{H-imidazol-}5\text{-yl]acetyl}\}$ amino-2-cyclohexylethylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.02-8.20(m, 13H), 5.42(s, 2H), 5.38(s, 2H), 4.10 (bs, 2H), 3.20(s, 2H), 3.02(s, 3H), 2.30 (bs, 2H), 1.40-2.00 (bs, 8H)

Example 492

N-Benzyl-N-benzylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

<Step 1>

N-Benzyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

Using the same method as described in Preparative Example 3, N-*t*-butoxycarbonyl-L-isoleucine was converted to N-(*t*-butoxycarbonyl)-L-isoleucine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 2,3-dichlorobenzylamine with benzylamine to give the title compound.

TLC : $R_f = 0.20$ (CH_2Cl_2 / MeOH = 9/1)

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 11H), 6.08(d, 1H), 5.06(dd, 2H), 3.90(m, 1H), 3.76(dd, 2H), 3.38(dd, 2H), 2.78(m, 3H), 1.48(m, 1H), 1.26(m, 1H), 1.04(m, 1H), 0.85(m, 6H)

<Step 2>

N-Benzyl-N-benzylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of N-benzyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added benzylisothiocyanate (0.1M in CH_2Cl_2 , 0.2ml, 0.02mmol). The reaction mixture was agitated for 3hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: $\text{CH}_2\text{Cl}_2/\text{MeOH}=9/1$, v/v) to give the title

compound as a white solid.

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.00-8.20(m, 16H), 5.80(t, 1H), 5.20-5.40(m, 3H), 4.78(t, 2H), 4.55(s, 2H), 4.15(m, 1H), 3.25(s, 2H), 3.18(dd, 2H), 1.62(m, 1H), 1.45(m, 1H), 1.05(m, 1H), 0.90(t, 6H)

Example 493-508

N-Benzyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 492 to give the title compounds.

Example 493

N-Benzyl-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.05-8.20(m, 15H), 5.30(m, 3H), 4.65-4.92(dd, 2H), 4.25(m, 1H), 3.38(s, 2H), 3.22(dd, 2H), 1.65(m, 1H), 1.45(m, 1H), 1.05(m, 1H), 0.90(t, 6H)

Example 494

N-Benzyl-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.00-8.20(m, 15H), 5.35(d, 2H), 4.95-5.22(m, 2H), 4.60(d, 1H), 4.20(m, 1H), 3.35(s, 2H), 3.20(dd, 2H), 1.64(m, 1H), 1.45(m, 1H), 1.05(m, 1H), 0.90(m, 6H)

Example 495

N-Benzyl-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-8.18(m, 15H), 5.34(d, 2H), 5.20(m, 1H), 4.60-4.95(dd, 2H), 4.18(m, 1H), 3.34(s, 2H), 3.22(dd, 2H), 1.65(m, 1H), 1.45(m, 1H), 1.08(m, 1H), 0.92(m, 6H)

Example 496

N-Benzyl-N-ethylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.02-8.20(m, 11H), 5.40(d, 2H), 5.20(m, 1H), 4.52(s, 2H), 4.10(m, 1H), 3.58(m, 2H), 3.32(s, 2H), 3.10(dd, 2H), 1.65(m, 1H), 1.42(m, 1H), 1.08(m, 1H), 1.05(t, 3H), 0.95(m, 6H)

Example 497

N-Benzyl-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-8.20(m, 15H), 5.35(d, 2H), 5.20(m, 1H), 4.62-4.95(dd, 2H), 4.22(m, 1H), 3.35(s, 2H), 3.20(dd, 2H), 1.62(m, 1H), 1.45(m, 1H), 1.10(m, 1H), 0.90(t, 6H)

Example 498

N-Benzyl-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.85-8.18(m, 15H), 5.38(d, 2H), 5.17(m, 1H), 4.58-4.98(dd, 2H), 4.20(m, 1H), 3.34(s, 2H), 3.22(dd, 2H), 1.60(m, 1H), 1.43(m, 1H), 1.08(m, 1H), 0.90(m, 6H)

Example 499

N-Benzyl-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.95-8.20(m, 15H), 5.35(d, 2H), 5.20(t, 1H), 4.60-4.95(dd, 2H), 4.20(m, 1H), 3.35(s, 2H), 3.20(dd, 2H), 1.60(m, 1H), 1.44(m, 1H), 1.06(m, 1H), 0.92(m, 6H)

Example 500

N-Benzyl-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.84-8.20(m, 15H), 5.36(d, 2H), 5.22(m, 1H), 4.60-4.88(dd, 2H), 4.18(m, 1H), 3.80(s, 3H), 3.38(s, 2H), 3.20(dd, 2H), 1.62(m, 1H), 1.45(m, 1H), 1.06(m, 1H), 0.92(t, 6H)

Example 501

N-Benzyl-N-methylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 11H), 5.72(t, 1H), 5.40(d, 2H), 5.18(t, 1H), 4.52(d, 2H), 4.15(m, 1H), 3.32(s, 2H), 3.12(dd, 1H), 3.08(d, 3H), 1.62(m, 1H), 1.44(m, 1H), 1.04(m, 1H), 0.95(t, 6H)

Example 502

N-Benzyl-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.90-8.18(m, 15H), 5.35(d, 2H), 5.08(m, 1H),

4.60-5.12(dd, 2H), 4.20(m, 1H), 3.35(s, 2H), 3.24(dd, 1H), 1.65(m, 1H), 1.45(m, 1H), 1.02(m, 1H), 0.95(m, 6H)

Example 503

N-Benzyl-N-allythiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-8.20(m, 11H), 5.60(m, 1H), 5.05-5.42(m, 2H), 4.95(m, 1H), 4.52(s, 2H), 4.18(m, 2H), 3.27(s, 2H), 3.08(dd, 1H), 1.38-1.65(m, 2H), 1.05(m, 1H), 0.82(m, 6H)

Example 504

N-Benzyl-N-(1-naphthylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-8.15(m, 18H), 5.28(m, 4H), 4.85(q, 1H), 4.24(m, 1H), 3.35(s, 2H), 3.10(dd, 1H), 1.35-1.60(m, 2H), 1.05(m, 1H), 0.88(m, 6H)

Example 505

N-Benzyl-N-phenylethylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR CDCl₃) : δ 6.90-8.20(m, 16H), 5.04-5.55(m, 5H), 4.38(s, 2H), 4.12(m, 1H), 3.90(m, 1H), 3.72(m, 1H), 3.25(s, 2H), 3.04(dd, 1H), 2.72(t, 2H), 1.38-1.62(m, 2H), 1.02(m, 1H), 0.84(m, 6H)

Example 506

N-Benzyl-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.02-8.20(m, 11H), 5.18-5.52(m, 5H), 4.46(s, 2H), 4.08(m, 1H), 3.62(m, 1H), 3.42(m, 1H), 3.35(s, 2H), 3.10(dd, 1H), 1.38-1.62(m, 2H), 1.35(m, 2H), 1.05(m, 2H), 0.90(m, 6H), 0.82(t, 3H)

Example 507

N-Benzyl-N-cyclohexylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.22(m, 11H), 4.85-5.10(m, 3H), 4.50(s, 2H), 4.10(m, 2H), 3.18(s, 2H), 3.12(dd, 1H), 0.92-1.73(m, 13H), 0.85(m, 6H)

Example 508

N-Benzyl-N-phenylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.18-8.22(m, 16H), 5.20-5.48(m, 3H), 4.80(q, 2H), 4.20(m, 2H), 3.38(s, 2H), 3.25(dd, 1H), 0.35-0.60(m, 2H), 1.03(m, 1H), 0.92(m, 6H)

Example 509

N-(Thiophen-2-ylmethyl)-N-benzylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

<Step 1>

N-(Thiophen-2-ylmethyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

Using the same method as described in Preparative Example 3, N-*t*-butoxycarbonyl-L-isoleucine was converted to N-(*t*-butoxycarbonyl)-L-

isoleucine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 2,3-dichlorobenzylamine with thiophen-2-ylmethylaniline to give the title compound.

TLC : $R_f = 0.20$ (CH_2Cl_2 / $\text{MeOH} = 10 / 1$)

$^1\text{H-NMR}$ (CDCl_3) : δ 8.20(d, 2H), 7.59(s, 1H), 7.15-7.40(m, 3H), 7.08(s, 1H), 6.84-7.00(m, 2H), 5.70-6.03(m, 1H), 5.34(s, 2H), 3.80-4.15(m, 3H), 3.38(s, 2H), 2.60-2.80(m, 2H), 1.82(bs, 1H), 1.22-1.65(m, 2H), 0.97-1.22(m, 1H), 0.75-0.95(m, 6H)

<Step 2>

N-(Thiophen-2-ylmethyl)-N-benzylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of N-(thiophen-2-ylmethyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added benzylisothiocyanate (0.1M in CH_2Cl_2 , 0.2ml, 0.02mmol). The reaction mixture was agitated for 4hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: $\text{CH}_2\text{Cl}_2/\text{MeOH}=9/1$, v/v) to give the title compound as a white solid.

$^1\text{H-NMR}$ (CDCl_3) : δ 6.84-8.20(m, 14H), 6.18-6.35(tt, 1H), 5.35(d, 2H), 5.00(m, 1H), 4.60-4.82(m, 4H), 4.18(m, 1H), 3.25(s, 2H), 3.20(dd, 1H), 1.38-1.62(m, 2H), 1.05(m, 1H), 0.95(d, 6H)

Examples 510-520

N-(Thiophen-2-ylmethyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]

acetyl}amino-3(S)-methylpentylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 509 to give the title compounds.

Example 510

N-(Thiophen-2-ylmethyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-8.18(m, 13H), 5.35(d, 2H), 5.02-5.20(m, 2H), 4.80(d, 1H), 4.32(m, 1H), 3.38(s, 2H), 3.32(dd, 1H), 1.40-1.62(m, 2H), 1.10(m, 1H), 0.97(d, 6H)

Example 511

N-(Thiophen-2-ylmethyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.05-8.18(m, 13H), 6.58,6.82(dd, 1H), 5.35(s, 2H), 4.63-4.88(m, 3H), 4.18(m, 1H), 3.36(s, 2H), 3.25(dd, 1H), 1.35-1.60(m, 2H), 1.12(m, 1H), 0.98(m, 6H)

Example 512

N-(Thiophen-2-ylmethyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.02-8.20(m, 13H), 5.18-5.42(m, 3H), 4.75(m, 2H), 4.20(m, 1H), 3.38(s, 2H), 3.28(dd, 1H), 1.35-1.60(m, 2H), 1.10(m, 1H), 0.98(m, 6H)

Example 513

N-(Thiophen-2-ylmethyl)-N-ethylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-i

imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.90-8.22(m, 9H), 5.86-6.05(tt, 1H), 5.40(m, 2H), 4.58-5.00(m, 3H), 4.16(m, 1H), 3.65(m, 2H), 3.34(s, 2H), 3.20(dd, 1H), 1.42-1.65(m, 2H), 1.16(m, 3H), 1.14(m, 1H), 0.97(m, 6H)

Example 514

N-(Thiophen-2-ylmethyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.02-8.20(m, 13H), 5.36(d, 2H), 5.00-5.22(m, 2H), 4.80(d, 1H), 4.28(m, 1H), 3.40(s, 2H), 3.32(dd, 1H), 1.35-1.64(m, 2H), 1.14(m, 1H), 0.97(d, 6H)

Example 515

N-(Thiophen-2-ylmethyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 13H), 5.35(d, 2H), 4.84-5.22(m, 2H), 4.70(d, 1H), 4.20(m, 1H), 3.38(s, 2H), 3.26(dd, 1H), 1.32-1.65(m, 2H), 1.12(m, 1H), 0.98(m, 6H)

Example 516

N-(Thiophen-2-ylmethyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-8.20(m, 13H), 5.36(m, 2H), 4.90-5.22(m, 2H), 4.72(d, 1H), 4.20(m, 1H), 3.38(s, 2H), 3.24(dd, 1H), 1.32-1.65(m, 2H), 1.12(m, 1H), 0.98(m, 6H)

Example 517

N-(Thiophen-2-ylmethyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.85-8.20(m, 13H), 5.38(m, 2H), 4.85-5.25(m, 2H), 4.75(d, 1H), 4.20(m, 1H), 3.80(s, 3H), 3.38(s, 2H), 3.26(dd, 1H), 1.40-1.65(m, 2H), 1.15(m, 1H), 0.98(d, 6H)

Example 518

N-(Thiophen-2-ylmethyl)-N-methylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.90-8.20(m, 9H), 6.06-6.30(tt, 1H), 5.40(m, 2H), 4.85(m, 2H), 4.58(dd, 1H), 4.10(m, 1H), 3.32(s, 2H), 3.22(dd, 1H), 3.08(d, 3H), 1.38-1.65(m, 2H), 1.12(m, 1H), 0.94(d, 6H)

Example 519

N-(Thiophen-2-ylmethyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.02-8.18(m, 13H), 5.20-5.58(m, 3H), 4.70(d, 2H), 4.18(m, 1H), 3.38(s, 2H), 3.28(d, 1H), 1.35-1.60(m, 2H), 1.10(m, 1H), 0.96(m, 6H)

Example 520

N-(Thiophen-2-ylmethyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.85-8.22(m, 9H), 5.88-6.15(tt, 1H), 5.38(d, 2H), 4.85-5.10(m, 2H), 4.62(t, 1H), 4.20(m, 2H), 3.35(s, 2H), 3.22(dd, 1H),

1.35-1.60(m, 2H), 1.10(m, 1H), 0.95(d, 6H)

Example 521

N-[2-(Thiophen-2-yl)ethyl]-N-benzylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

<Step 1>

N-[2-(Thiophen-2-yl)ethyl]-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

Using the same method as described in Preparative Example 3, N-*t*-butoxycarbonyl-L-isoleucine was converted to N-(*t*-butoxycarbonyl)-L-isoleucine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 2,3-dichlorobenzylamine with 2-(thiophen-2-yl)ethylamine to give the title compound.

TLC : R_f = 0.20 (CH₂Cl₂ / MeOH = 10 / 1)

¹H-NMR (CDCl₃) : δ 8.20(d, 2H), 7.59(s, 1H), 7.15-7.40(m, 3H), 7.08(s, 1H), 6.84-7.00(m, 2H), 5.70-6.03(m, 1H), 5.34(s, 2H), 3.80-4.15(m, 3H), 3.38(s, 2H), 2.60-2.80(m, 2H), 1.82 (bs, 1H), 1.22-1.65(m, 2H), 0.97-1.22(m, 1H), 0.75-0.95(m, 6H)

<Step 2>

N-[2-(Thiophen-2-yl)ethyl]-N-benzylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of N-[2-(Thiophen-2-yl)ethyl]-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added benzylisothiocyanate (0.1M in

CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 4hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: CH₂Cl₂/MeOH=9/1, v/v) to give the title compound as a white solid.

¹H-NMR (CDCl₃) : δ 6.75-8.20(m, 14H), 5.25(d, 2H), 4.95 (bs, 1H), 4.20(m, 1H), 4.05(m, 1H), 3.64 (bs, 1H), 3.25-3.34 (bs, 4H), 3.20(dd, 1H), 1.30-1.70(m, 2H), 1.10(m, 1H), 0.90(m, 6H)

Examples 522-525

N-[2-(Thiophen-2-yl)ethyl]-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 521 to give the title compounds.

Example 522

N-[2-(Thiophen-2-yl)ethyl]-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.85-8.15(m, 13H), 5.30(dd, 2H), 4.86 (bs, 1H), 4.16(m, 1H), 3.95 (bs, 1H), 3.60(m, 1H), 3.28(s, 2H), 3.18(m, 2H), 3.05(dd, 1H), 1.30-1.70(m, 2H), 1.10(m, 1H), 0.90(m, 6H)

Example 523

N-[2-(Thiophen-2-yl)ethyl]-N-ethylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.80-8.20(m, 9H), 5.40(m, 2H), 4.95 (bs, 1H), 4.08(m, 1H), 3.35-3.80(m, 4H), 3.26(s, 2H), 2.98(m, 2H), 2.86(dd, 1H),

1.30-1.70(m, 2H), 1.10(m, 1H), 0.90(m, 6H)

Example 524

N-[2-(Thiophen-2-yl)ethyl]-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.85-8.10(m, 13H), 5.30(d, 2H), 5.22 (bs, 1H), 4.80 (bs, 1H), 4.18(m, 2H), 4.02(m, 1H), 3.55(m, 1H), 3.30(s, 2H), 3.18(m, 2H), 3.05(dd, 1H), 1.30-1.70(m, 2H), 1.05(m, 1H), 0.92(m, 6H)

Example 525

N-[2-(Thiophen-2-yl)ethyl]-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.85-8.20(m, 13H), 5.35(m, 2H), 5.00 (bs, 1H), 4.15(m, 1H), 3.95(m, 1H), 3.65(m, 1H), 3.28(s, 2H), 3.18(m, 2H), 3.02(dd, 1H), 1.30-1.70(m, 2H), 1.05(m, 1H), 0.92(m, 6H)

Example 526

N-(2-Trifluoromethylbenzyl)-N-benzylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

<Step 1>

N-(2-Trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

Using the same method as described in Preparative Example 3, N-*t*-butoxycarbonyl-L-isoleucine was converted to N-*t*-butoxycarbonyl-L-isoleucine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing

2,3-dichlorobenzylamine and 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride with 2-trifluoromethylbenzylamine and 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride, respectively, to give the title compound.

TLC : $R_f = 0.40$ (CH_2Cl_2 / $\text{MeOH} = 10 / 1$)

$^1\text{H-NMR}$ (CDCl_3) : δ 7.6(m, 3H), 7.5(m, 3H), 7.4(m, 1H), 7.1(d, 2H), 7.0(s, 1H), 5.3(s, 2H), 4.0(m, 3H), 3.4(s, 2H), 2.7(m, 2H), 1.0-1.5(m, 3H), 0.8-0.9(m, 6H)

<Step 2>

N-(2-Trifluoromethylbenzyl)-N-benzylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of N-(2-trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added benzylisothiocyanate (0.1M in CH_2Cl_2 , 0.2ml, 0.02mmol). The reaction mixture was agitated for 4hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: $\text{CH}_2\text{Cl}_2/\text{MeOH}=9/1$, v/v) to give the title compound as a white solid.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-7.68(m, 15H), 5.28(d, 2H), 4.62-5.18(m, 5H), 4.12(m, 1H), 3.24(s, 2H), 3.05(dd, 1H), 1.38-1.70 (bs, 2H), 1.06(m, 1H), 0.88(m, 6H)

Examples 527-580

N-(2-Trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine was reacted with the

corresponding isothiocyanates under the same condition as described in <Step 2> of Example 526 to give the title compounds.

Example 527

N-(2-Trifluoromethylbenzyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.75(m, 14H), 5.25(d, 2H), 4.98-5.35 (bs, 2H), 4.86(d, 1H), 4.23(m, 1H), 3.35(d, 2H), 3.16(dd, 1H), 1.35-1.65 (bs, 2H), 1.04(m, 1H), 0.90(m, 6H)

Example 528

N-(2-Trifluoromethylbenzyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.88-7.70(m, 14H), 5.52 (bs, 1H), 5.22(s, 2H), 4.78(dd, 2H), 4.15(m, 1H), 3.35(s, 2H), 3.10(dd, 1H), 1.35-1.65 (bs, 2H), 1.04(m, 1H), 0.92(m, 6H)

Example 529

N-(2-Trifluoromethylbenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.88-7.70(m, 14H), 5.45 (bs, 1H), 5.25(d, 2H), 4.80(dd, 2H), 4.18(m, 1H), 3.32(s, 2H), 3.13(dd, 1H), 1.30-1.68 (bs, 2H), 1.02(m, 1H), 0.86(m, 6H)

Example 530

N-(2-Trifluoromethylbenzyl)-N-ethylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.95-7.78(m, 10H), 5.45 (bs, 1H), 5.84-6.02 (bs, 1H), 5.36(dd, 2H), 5.02 (bs, 1H), 4.64-4.95(dd, 2H), 4.08(m, 1H), 3.60(m, 2H), 3.35(s, 2H), 3.04(dd, 1H), 1.30-1.70 (bs, 2H), 1.03(m, 2H), 0.85(m, 6H)

Example 531

N-(2-Trifluoromethylbenzyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.88-7.75(m, 14H), 5.25(d, 2H), 4.98-5.24 (bs, 2H), 4.64(d, 1H), 4.20(m, 1H), 3.35(s, 2H), 3.12(dd, 1H), 1.30-1.70 (bs, 2H), 1.05(m, 1H), 0.85(m, 6H)

Example 532

N-(2-Trifluoromethylbenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.80-7.80(m, 14H), 5.44 (bs, 1H), 5.24(s, 2H), 4.83(dd, 2H), 4.17(m, 1H), 3.37(s, 2H), 3.14(dd, 1H), 1.30-1.70 (bs, 2H), 1.05(m, 1H), 0.85(m, 6H)

Example 533

N-(2-Trifluoromethylbenzyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.75(m, 14H), 5.38 (bs, 1H), 5.25(m, 2H), 4.75-5.02 (bs, 2H), 4.15(m, 1H), 3.35(s, 2H), 3.12(dd, 1H), 1.30-1.75 (bs, 2H), 1.05(m, 1H), 0.90(m, 6H)

Example 534

N-(2-Trifluoromethylbenzyl)-N-methylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.85-7.75(m, 10H), 6.25-6.44 (bs, 1H), 5.35(d, 2H), 4.80-5.10 (bs, 2H), 4.63(dd, 1H), 4.08(m, 1H), 3.32(s, 2H), 3.08(s, 3H), 3.00(dd, 1H), 1.30-1.75 (bs, 2H), 1.05(m, 1H), 0.88(m, 6H)

Example 535

N-(2-Trifluoromethylbenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.90-7.75(m, 14H), 5.62 (bs, 1H), 5.25(s, 2H), 4.78(dd, 2H), 4.13(m, 1H), 3.32(s, 2H), 3.14(dd, 1H), 1.30-1.75 (bs, 2H), 1.05(m, 1H), 0.90(m, 6H)

Example 536

N-(2-Trifluoromethylbenzyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.75(m, 10H), 6.00-6.20 (bs, 1H), 5.78(m, 1H), 5.35(dd, 2H), 5.05(d, 2H), 4.62-4.95(dd, 2H), 4.24(m, 1H), 4.15(m, 1H), 3.30(s, 2H), 3.08(dd, 1H), 1.30-1.70(m, 2H), 1.05(m, 1H), 0.86(m, 6H)

Example 537

N-(2-Trifluoromethylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.8(d, 1H), 7.6(d, 2H), 7.5(m, 2H), 7.3(m, 2H),

7.1(s, 1H), 6.9(d, 2H), 5.3(m, 2H), 4.9(d, 2H), 4.2(m, 1H), 3.8(s, 2H), 3.4(s, 2H), 3.2(dd, 2H), 1.0-1.8(m, 3H), 0.9(m, 6H)

Example 538

N-(2-Trifluoromethylbenzyl)-N-(*t*-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.78(m, 10H), 5.32(m, 3H), 4.68 (bs, 2H), 4.10(m, 1H), 3.35(s, 2H), 3.02(dd, 1H), 1.30-1.70(m, 2H), 1.05(m, 1H), 0.88(m, 6H)

Example 539

N-(2-Trifluoromethylbenzyl)-N-(1-adamantylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.60-7.75(m, 3H), 7.35-7.59(m, 4H), 7.02-7.22(m, 3H), 5.39(m, 2H), 5.25(s, 1H), 5.12(d, 1H), 4.70(s, 2H), 4.10(m, 1H), 3.35(s, 2H) 2.95(dd, 1H), 1.85-2.10(m, 9H), 1.60(m, 7H), 1.10(m, 2H), 0.90(m, 6H)

Example 540

N-(2-Trifluoromethylbenzyl)-N-(4-azidophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.73(d, 1H), 7.60(d, 4H), 7.45(d, 1H), 7.25-7.39(m, 3H), 6.90-7.18(m, 6H), 5.20-5.70(m, 4H), 4.80(m, 2H), 4.18(m, 1H), 3.40(s, 2H), 3.12(dd, 1H), 1.65(m, 1H), 1.00-1.50(m, 2H), 0.90(t, 6H)

Example 541

N-(2-Trifluoromethylbenzyl)-N-(2-biphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

enzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.50-7.65(m, 5H), 7.20-7.40(m, 9H), 7.15(m, 3H), 7.05(s, 1H), 6.85(m, 1H), 6.00(s, 1H), 5.25(s, 2H), 4.65(m, 2H), 4.10(m, 1H), 3.38(s, 2H), 3.00(dd, 1H), 1.60(m, 1H), 0.95-1.45(m, 2H), 0.85(m, 6H)

Example 542

N-(2-Trifluoromethylbenzyl)-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.75(s, 1H), 7.65(d, 3H), 7.40-7.55(m, 2H), 7.20(d, 3H), 7.05(s, 1H), 5.90-6.20(m, 2H), 5.40(m, 2H), 4.90-5.10(m, 2H), 4.65(m, 1H), 4.10(m, 1H), 3.40-3.70(m, 2H), 3.20(s, 2H), 3.05(dd, 1H), 1.62(m, 1H), 1.45(m, 3H), 1.30(m, 1H), 1.15(m, 3H), 0.85(m, 6H), 0.80(m, 3H)

Example 543

N-(2-Trifluoromethylbenzyl)-N-(*t*-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.75(s, 1H), 7.65(d, 2H), 7.54(s, 1H), 7.40-7.50(m, 3H), 7.20(d, 2H), 7.05(s, 1H), 5.20-5.40(m, 4H), 4.70(m, 2H), 4.65(m, 1H), 4.10(m, 1H), 3.35(s, 2H), 3.00(dd, 1H), 1.40-1.62(m, 2H), 1.35(s, 9H), 1.10(m, 1H), 0.85(m, 6H)

Example 544

N-(2-Trifluoromethylbenzyl)-N-(2-chloroethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.70(s, 1H), 7.65(d, 2H), 7.54(s, 1H), 7.25-7.52(m, 3H), 7.20(d, 2H), 7.05(s, 1H), 5.38(s, 2H), 4.70(s, 2H), 4.00(m, 3H), 3.40(m, 1H), 3.35(s, 2H), 2.95(dd, 1H), 1.62(m, 1H), 1.35(m, 3H), 1.10(m, 1H), 0.85(m, 6H)

Example 545

N-(2-Trifluoromethylbenzyl)-N-(3-chloro-4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.70(d, 1H), 7.60(m, 3H), 7.25-7.50(m, 4H), 7.18(m, 4H), 7.05(s, 1H), 5.20-5.40(m, 3H), 4.80(m, 2H), 4.20(m, 1H), 3.40(s, 2H), 3.15(dd, 1H), 2.30(s, 3H), 1.65(m, 1H), 1.10-1.55(m, 2H), 0.85(m, 6H)

Example 546

N-(2-Trifluoromethylbenzyl)-N-cyclohexylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.80(s, 1H), 7.70(s, 1H), 7.65(d, 2H), 7.40-7.60(m, 2H), 7.10-7.30(m, 4H), 5.60(m, 1H), 5.40(s, 2H), 5.00(m, 2H), 4.65(m, 1H), 4.15(m, 2H), 3.40(s, 2H), 3.15(dd, 1H), 1.80(m, 2H), 1.20-1.62(m, 6H), 1.10(s, 3H), 0.85(m, 6H)

Example 547

N-(2-Trifluoromethylbenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.75(d, 1H), 7.60(d, 2H), 7.50(m, 1H), 7.20-7.40(m, 3H), 7.15(d, 2H), 7.00(s, 1H), 6.90(d, 1H), 5.30(s, 2H), 4.90(m, 2H), 4.30(m, 1H), 3.38(s, 2H), 3.20(dd, 1H), 1.64(m, 1H),

1.10-1.40(m, 2H), 0.85(t, 6H)

Example 548

N-(2-Trifluoromethylbenzyl)-N-(4-isopropylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.65(m, 2H), 7.60(m, 3H), 7.30-7.50(m, 3H), 7.00-7.20(m, 6H), 5.70(bs, 1H), 5.35(m, 2H), 4.80(m, 2H), 4.20(m, 1H), 3.40(s, 2H), 3.10(dd, 1H), 2.90(m, 1H), 1.65(m, 1H), 1.40(m, 1H), 1.20(d, 6H), 1.15(m, 1H), 0.85(t, 6H)

Example 549

N-(2-Trifluoromethylbenzyl)-N-(3-methoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.75(s, 1H), 7.70(d, 2H), 7.45(m, 2H), 7.25(d, 2H), 7.10(s, 2H), 6.90(d, 1H), 5.75(bs, 1H), 5.45(d, 2H), 5.10(m, 1H), 4.70(m, 2H), 4.10(m, 1H), 3.70(m, 2H), 3.50(t, 1H), 3.40(s, 3H), 3.34(m, 1H), 2.95(dd, 1H), 2.80(d, 2H), 1.80(m, 2H), 1.64(m, 1H), 1.10-1.40(m, 2H), 0.90(d, 6H)

Example 550

N-(2-Trifluoromethylbenzyl)-N-(2-naphthylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.60-7.80(m, 5H), 7.25-7.60(m, 9H), 7.00(m, 3H), 5.60(m, 1H), 5.20(s, 2H), 4.90(m, 2H), 4.20(m, 1H), 3.38(s, 2H), 3.15(dd, 1H), 1.64(m, 1H), 1.00-1.40(m, 2H), 0.85(t, 6H)

Example 551

N-(2-Trifluoromethylbenzyl)-N-ethoxycarbonylmethylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(m, 3H), 7.45(m, 3H), 7.20(m, 3H), 7.00(s, 1H), 5.35(s, 5H), 4.70(m, 1H), 4.35(m, 2H), 4.16(q, 2H), 3.38(s, 2H), 3.05(dd, 1H), 1.36-1.64(m, 2H), 1.25(t, 3H), 1.10(m, 1H), 0.85(t, 6H)

Example 552

N-(2-Trifluoromethylbenzyl)-N-(4-methylthiophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.75(d, 1H), 7.60(d, 2H), 7.50(m, 3H), 7.15-7.38(m, 5H), 7.10(d, 2H), 7.00(s, 1H), 5.42(m, 1H), 5.30(s, 2H), 4.80(m, 2H), 3.90-4.20(m, 2H), 3.38(s, 2H), 3.15(dd, 1H), 2.45(s, 3H), 1.64(m, 1H), 1.00-1.40(m, 2H), 0.85(t, 6H)

Example 553

N-(2-Trifluoromethylbenzyl)-N-isopropylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.75(s, 2H), 7.65(d, 2H), 7.50(m, 2H), 7.22(d, 3H), 7.05(s, 1H), 5.90(bs, 1H), 5.40(m, 2H), 5.00(m, 2H), 4.65(m, 1H), 4.15(m, 1H), 3.50(m, 1H), 3.38(s, 2H), 3.25(m, 1H), 3.10(dd, 1H), 1.52-1.80(m, 2H), 1.40(m, 1H), 1.10(m, 1H), 0.90(m, 6H), 0.75(p, 6H)

Example 554

N-(2-Trifluoromethylbenzyl)-N-(2-methoxyethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.75(s, 1H), 7.65(d, 3H), 7.45(m, 2H), 7.15-7.30(m,

3H), 7.10(s, 1H), 6.15(bd, 1H), 5.80(bs, 1H), 5.30(m, 2H), 4.80-5.10(m, 2H), 4.65(m, 1H), 4.20(m, 1H), 3.74(m, 2H), 3.40(s, 4H), 3.20(d, 3H), 1.40-1.64(m, 2H), 1.10(m, 1H), 0.87(d, 6H)

Example 555

N-(2-Trifluoromethylbenzyl)-N-cyclopropylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.75(s, 1H), 7.65(d, 3H), 7.45(m, 2H), 7.10-7.25(m, 4H), 6.55(bd, 1H), 5.80(bs, 1H), 5.40(s, 2H), 5.15(m, 1H), 4.80(m, 1H), 4.65(m, 2H), 4.05(m, 1H), 3.40(s, 2H), 3.05(m, 2H), 1.60(m, 1H), 1.10-1.45(m, 2H), 0.85(t, 6H), 0.80(m, 2H), 0.40(m, 2H)

Example 556

N-(2-Trifluoromethylbenzyl)-N-[2-(dimethylamino)ethylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.75(s, 1H), 7.65(d, 2H), 7.55(s, 1H), 7.45(t, 2H), 7.20(d, 3H), 7.00(s, 1H), 5.40(d, 2H), 4.70-5.10(m, 3H), 4.20(m, 1H), 3.64(m, 2H), 3.40(m, 2H), 3.15(dd, 1H), 2.65(m, 2H), 2.20(bs, 4H), 1.35-1.65(m, 2H), 1.28(s, 1H), 1.10(m, 1H), 0.87(t, 6H)

Example 557

N-(2-Trifluoromethylbenzyl)-N-(3-ethoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.80(s, 1H), 7.65(d, 2H), 7.45(m, 2H), 7.25(d, 2H), 7.10(s, 2H), 6.85(m, 1H), 5.80(bs, 1H), 5.45(d, 2H), 5.10(m, 1H), 4.60-4.90(m, 2H), 4.10(m, 1H), 3.74(q, 2H), 3.30-3.56(m, 4H), 3.15(m, 2H), 1.30-1.84(m, 4H), 1.00-1.25(m, 3H), 0.84(m, 10H)

Example 558

N-(2-Trifluoromethylbenzyl)-N-[4-(dimethylamino)phenylthiocarbamoyl]-2(S)-
-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.70(m, 2H), 7.58(d, 2H), 7.40(m, 3H), 7.15(d, 2H), 7.05(m, 2H), 6.60(d, 2H), 6.20(bs, 1H), 5.30(m, 2H), 4.80(m, 1H), 4.20(m, 1H), 3.40(s, 2H), 3.10(dd, 1H), 2.90(s, 6H), 1.60(m, 1H), 1.10-1.44(m, 2H), 0.87(t, 6H)

Example 559

N-(2-Trifluoromethylbenzyl)-N-(n-pentylthiocarbamoyl)-2(S)-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.65(m, 3H), 7.45(m, 2H), 7.22(d, 3H), 7.05(m, 2H), 5.50-6.00(m, 2H), 5.40(m, 2H), 4.80-5.10(m, 2H), 4.65(m, 1H), 4.10(m, 1H), 3.64(m, 1H), 3.40(s, 4H), 3.10(dd, 1H), 1.40-1.64(m, 2H), 1.10-1.30(m, 2H), 0.87(m, 6H), 0.60-0.84(m, 6H)

Example 560

N-(2-Trifluoromethylbenzyl)-N-(4-nitrophenylthiocarbamoyl)-2(S)-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 8.10(m, 2H), 7.52-7.75(m, 6H), 7.28-7.50(m, 2H), 7.12(d, 2H), 7.00(s, 1H), 6.85(d, 1H), 5.70-5.90(m, 1H), 5.30(s, 2H), 4.80(m, 1H), 4.55(bs, 1H), 4.10(m, 2H), 3.40(s, 2H), 3.10(dd, 1H), 1.64(m, 1H), 1.10-1.50(m, 2H), 0.87(m, 6H)

Example 561

N-(2-Trifluoromethylbenzyl)-N-(*t*-octylthiocarbamoyl)-2(S)-[1-(4-cyanobenz

yl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.70(m, 2H), 7.65(d, 2H), 7.50(s, 1H), 7.45(t, 2H), 7.20(d, 2H), 7.05(s, 1H), 5.40(d, 2H), 5.25(s, 1H), 4.70(m, 2H), 4.10(m, 1H), 3.34(q, 2H), 3.00(m, 1H), 2.10(m, 2H), 1.60(m, 1H), 1.35(d, 6H), 1.05(m, 2H), 0.87(m, 6H), 0.80(m, 9H)

Example 562

N-(2-Trifluoromethylbenzyl)-N-phenylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.70(d, 1H), 7.57(m, 4H), 7.20-7.50(m, 7H), 7.10(d, 2H), 7.00(s, 1H), 5.40-5.60(m, 2H), 5.24(s, 1H), 4.80-5.00(m, 2H), 4.20(m, 1H), 3.40(s, 2H), 3.10(dd, 1H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.87(m, 6H)

Example 563

N-(2-Trifluoromethylbenzyl)-N-(n-propylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.65(m, 3H), 7.45(m, 2H), 7.22(d, 3H), 7.05(s, 2H), 6.10(m, 1H), 5.40(m, 2H), 4.80-5.10(m, 2H), 4.65(m, 1H), 4.10(m, 1H), 3.54(m, 2H), 3.40(s, 2H), 3.10(dd, 1H), 1.40-1.64(m, 3H), 1.00-1.30(m, 2H), 0.87(t, 6H), 0.75(m, 3H)

Example 564

N-(2-Trifluoromethylbenzyl)-N-(2-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.75(d, 1H), 7.60(m, 4H), 7.45(m, 3H), 7.15(m,

6H), 7.00(s, 1H), 5.30(m, 3H), 4.85(m, 2H), 4.20(m, 1H), 3.40(s, 2H), 3.20(dd, 1H), 2.05(d, 3H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.87(t, 6H)

Example 565

N-(2-Trifluoromethylbenzyl)-N-(2,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.75(m, 2H), 7.60(m, 3H), 7.40(m, 2H), 7.15(d, 2H), 7.05(s, 1H), 6.95(m, 3H), 5.95(bs, 1H), 5.30(m, 2H), 4.85(m, 2H), 4.20(m, 1H), 3.40(s, 2H), 3.20(dd, 1H), 2.30(s, 3H), 2.00(d, 3H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.87(t, 6H)

Example 566

N-(2-Trifluoromethylbenzyl)-N-(3,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.75(d, 1H), 7.60(m, 3H), 7.40(m, 2H), 7.15(d, 3H), 7.05(s, 1H), 6.95(d, 2H), 5.40(m, 3H), 4.80(m, 2H), 4.20(m, 1H), 3.40(s, 2H), 3.15(dd, 1H), 2.20(d, 6H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.87(t, 6H)

Example 567

N-(2-Trifluoromethylbenzyl)-N-(3-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.70(m, 2H), 7.55(m, 4H), 7.35(m, 1H), 6.95-7.20(m, 7H), 6.20(s, 1H), 5.30(m, 2H), 4.80(m, 2H), 4.20(m, 1H), 3.40(s, 2H), 3.15(dd, 1H), 2.30(s, 3H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.87(t, 6H)

Example 568

N-(2-Trifluoromethylbenzyl)-N-(4-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.70(d, 1H), 7.60(m, 4H), 7.45(m, 3H), 7.30(m, 3H), 7.10(d, 3H), 7.00(s, 1H), 5.60(m, 1H), 5.20(m, 2H), 4.80(m, 2H), 4.20(m, 1H), 3.40(s, 2H), 3.15(dd, 1H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.87(t, 6H)

Example 569

N-(2-Trifluoromethylbenzyl)-N-(2-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.75(m, 2H), 7.60(m, 4H), 7.40(m, 4H), 7.15(m, 4H), 7.00(s, 1H), 5.80(bs, 1H), 5.30(m, 2H), 4.85(m, 2H), 4.20(m, 1H), 3.40(s, 2H), 3.20(dd, 1H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.87(t, 6H)

Example 570

N-(2-Trifluoromethylbenzyl)-N-(3-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.75(d, 1H), 7.60(m, 4H), 7.20-7.50(m, 5H), 7.15(m, 4H), 7.00(s, 1H), 5.65(m, 1H), 5.30(m, 2H), 4.80(m, 2H), 4.20(m, 1H), 3.40(s, 2H), 3.15(dd, 1H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.87(t, 6H)

Example 571

N-(2-Trifluoromethylbenzyl)-N-(4-dimethylamino-1-naphthylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.20(d, 1H), 7.75(d, 1H), 7.20-7.60(m, 9H), 7.00(m, 4H), 5.85(s, 1H), 5.30(m, 2H), 5.20(d, 2H), 4.95(m, 1H), 4.30(m, 1H), 3.40(s, 2H), 3.20(dd, 1H), 2.90(s, 6H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.87(t, 6H)

Example 572

N-(2-Trifluoromethylbenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.25(d, 1H), 7.80(d, 1H), 7.60(m, 6H), 7.30(m, 1H), 7.10(m, 4H), 6.95(t, 1H), 6.80(d, 1H), 5.30(m, 3H), 4.85(m, 2H), 4.30(m, 1H), 3.55(s, 3H), 3.40(s, 2H), 3.20(dd, 1H), 2.05(d, 3H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.92(d, 6H)

Example 573

N-(2-Trifluoromethylbenzyl)-N-(4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.75(d, 1H), 7.60(d, 3H), 7.40(m, 3H), 7.15(m, 5H), 7.00(s, 1H), 5.30(m, 3H), 4.75-5.10(m, 3H), 4.20(m, 1H), 3.40(s, 2H), 3.10(dd, 1H), 2.35(s, 3H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.87(t, 6H)

Example 574

N-(2-Trifluoromethylbenzyl)-N-phenethylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(d, 2H), 7.60(s, 1H), 7.40(t, 2H), 7.30(m, 2H), 7.20(d, 2H), 7.15(m, 4H), 7.00(m, 2H), 5.70-6.20(m, 2H), 5.30(m, 2H),

4.85(m, 2H), 4.60(m, 1H), 4.10(m, 1H), 3.80(m, 2H), 3.40(s, 2H), 3.05(m, 1H), 2.80(m, 2H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.87(t, 6H)

Example 575

N-(2-Trifluoromethylbenzyl)-N-(2-methoxypyridin-4-ylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.95(m, 1H), 7.75(m, 2H), 7.60(d, 3H), 7.45(m, 1H), 7.30(m, 2H), 7.15(d, 2H), 7.00(s, 1H), 6.70(d, 1H), 6.00(bs, 1H), 5.30(m, 2H), 4.80(m, 2H), 4.20(m, 1H), 3.85(s, 3H), 3.40(s, 2H), 3.20(dd, 1H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.87(t, 6H)

Example 576

N-(2-Trifluoromethylbenzyl)-N-[3-(dimethylamino)propylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.75(m, 1H), 7.65(d, 2H), 7.45(m, 3H), 7.20(d, 2H), 7.10(m, 1H), 7.00(s, 1H), 5.40(d, 2H), 4.80(m, 3H), 4.20(m, 1H), 3.70(m, 3H), 3.35(m, 2H), 2.95(m, 1H), 2.55(m, 2H), 2.00(m, 6H), 1.64(m, 1H), 1.00-1.50(m, 5H), 0.87(m, 6H)

Example 577

N-(2-Trifluoromethylbenzyl)-N-(2-hydroxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(s, 1H), 7.60(d, 3H), 7.55(m, 4H), 7.40(d, 2H), 7.15(d, 3H), 7.00(s, 1H), 6.85(m, 1H), 6.00(bs, 1H), 5.25(s, 2H), 3.95(m, 1H), 3.90(s, 2H), 3.40(s, 2H), 2.65(m, 2H), 1.85(bs, 2H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.87(m, 6H)

Example 578

N-(2-Trifluoromethylbenzyl)-N-(4-hydroxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.70(d, 2H), 7.25-7.60(m, 5H), 7.10(m, 2H), 6.95(m, 3H), 6.60(d, 2H), 5.30(m, 3H), 4.80(m, 2H), 4.20(m, 1H), 3.40(m, 2H), 3.10(d, 1H), 1.64(m, 1H), 1.00-1.50(m, 3H), 0.87(t, 6H)

Example 579

N-(2-Trifluoromethylbenzyl)-N-(2-chloropyridin-5-ylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 8.30(d, 1H), 8.00(t, 1H), 7.75(d, 1H), 7.60(d, 2H), 7.45(m, 2H), 7.30(m, 2H), 7.10(d, 2H), 7.00(s, 1H), 6.60(m, 1H), 5.75(m, 1H), 5.25(m, 2H), 4.80(m, 1H), 4.10(m, 1H), 3.40(s, 2H), 3.20(dd, 1H), 1.64(m, 1H), 1.00-1.50(m, 2H), 0.87(t, 6H)

Example 580

N-(2-Trifluoromethylbenzyl)-N-cyclopentylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 7.80(s, 1H), 7.65(d, 3H), 7.45(m, 2H), 7.20(d, 3H), 7.10(s, 1H), 5.90(bs, 1H), 5.40(s, 2H), 5.00(m, 2H), 4.60(m, 2H), 4.10(m, 1H), 3.40(s, 2H), 3.10(dd, 1H), 1.95(m, 2H), 1.00-1.80(m, 9H), 0.87(t, 6H)

Example 581

N-(2-Trifluoromethylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine
hydrochloride

Hydrogen chloride gas was bubbled through a solution of Example 537 in ethyl acetate while stirring until a white slurry appeared. It was crystallized from diethylether to produce a solid, which was then filtered and recrystallized from ethanol to give the title compound as a white solid.

¹H-NMR (CD₃OD) : δ 9.18(s, 1H), 7.85(m, 4H), 7.80(s, 1H), 7.64(m, 4H), 7.39(d, 2H), 7.02(d, 2H), 5.80(s, 2H), 5.35(dd, 2H), 4.30(m, 1H), 3.92-3.98(m, 5H), 3.50(s, 2H), 1.20-1.82(m, 3H), 1.06(m, 6H)

Example 582

N-(2-Trifluoromethylbenzyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

<Step 1>

N-(2-Trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

Using the same method as described in Preparative Example 3, N-*t*-butoxycarbonyl-L-alanine was converted to N-(*t*-butoxycarbonyl)-L-alanine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 2,3-dichlorobenzylamine and 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride with 2-trifluoromethylbenzylamine and 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride, respectively, to give the title compound.

¹H-NMR (CDCl₃) : δ 7.00-7.66(m, 10H), 6.29(d, 1H), 5.27(s, 2H), 4.00(m, 1H), 3.90(s, 2H), 3.35(s, 2H), 2.64(d, 2H), 1.10(d, 3H)

<Step 2>

N-(2-Trifluoromethylbenzyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

To a solution of N-(2-trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added allylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 2hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: CH₂Cl₂/MeOH=9/1, v/v) to give the title compound as a white solid.

¹H-NMR (CDCl₃) : δ 6.99-7.71(m, 9H), 6.51 (bs, 1H), 5.84(m, 1H), 5.30(s, 2H), 5.15(d, 1H), 5.06(m, 2H), 4.70(d, 1H), 4.50(d, 1H), 4.29 (bs, 2H), 4.09(m, 1H), 3.32(s, 2H), 2.96(dd, 1H), 1.17(d, 3H)

Examples 583-625

N-(2-trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 582 to give the title compounds.

Example 583

N-(2-Trifluoromethylbenzyl)-N-benzylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.95-7.67(m, 14H), 5.36(d, 1H), 5.22(s, 1H), 4.86(d, 2H), 4.72(d, 1H), 4.68(s, 1H), 4.08(m, 1H), 3.26(s, 2H), 2.98(dd,

1H), 1.16(d, 3H)

Example 584

N-(2-Trifluoromethylbenzyl)-N-(2-biphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.95-7.62(m, 18H), 5.25(d, 1H), 5.21(s, 2H), 4.63(d, 1H), 4.43(s, 1H), 3.94 (bs, 1H), 3.27(s, 2H), 2.83(dd, 1H), 1.11(d, 3H)

Example 585

N-(2-Trifluoromethylbenzyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.99-7.73(m, 13H), 5.57 (bs, 1H), 5.28(d, 1H), 5.24(s, 2H), 4.83(d, 1H), 4.72(bs, 1H), 4.28(m, 1H), 3.34(s, 2H), 3.08(dd, 1H), 1.21(d, 3H)

Example 586

N-(2-Trifluoromethylbenzyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 9.17 (bs, 1H), 6.94-7.70(m, 13H), 5.95(d, 1H), 5.29(s, 2H), 4.77(d, 1H), 4.32(m, 1H), 4.09(m, 1H), 3.33(s, 2H), 2.96(dd, 1H), 1.24(d, 3H)

Example 587

N-(2-Trifluoromethylbenzyl)-N-(4-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.95 (bs, 1H), 6.95-7.71(m, 13H), 5.87(d, 1H), 5.24(s, 2H), 4.79(d, 1H), 4.36(m, 1H), 4.10(m, 1H), 3.34(s, 2H), 2.97(dd, 1H), 1.23(d, 3H)

Example 588

N-(2-Trifluoromethylbenzyl)-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-7.71(m, 9H), 6.27 (bs, 1H), 5.33(s, 2H), 5.21(d, 1H), 4.69(d, 1H), 4.62(m, 1H), 4.08(m, 1H), 3.60(m, 2H), 3.33(s, 2H), 2.97(dd, 1H), 1.49(m, 2H), 1.26(m, 2H), 1.18(d, 3H), 0.85 (t, 3H)

Example 589

N-(2-Trifluoromethylbenzyl)-N-isobutylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-7.72(m, 9H), 6.18 (bs, 1H), 5.34(s, 2H), 5.22(d, 1H), 4.76(m, 1H), 4.71(d, 1H), 4.10(m, 1H), 3.44(m, 2H), 3.33(s, 2H), 3.02(dd, 1H), 1.84(m, 1H), 1.18(d, 3H), 0.76(d, 6H)

Example 590

N-(2-Trifluoromethylbenzyl)-N-(2-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.99-7.73(m, 13H), 5.53(d, 1H), 5.24(s, 2H), 4.88(d, 1H), 4.72(m, 1H), 4.26(m, 1H), 3.34(s, 2H), 3.08(dd, 1H), 1.21(d, 3H)

Example 591

N-(2-Trifluoromethylbenzyl)-N-(3-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cy

anobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 9.18 (bs, 1H), 6.94-7.70(m, 13H), 5.94(d, 1H), 5.28(s, 2H), 4.77(d, 1H), 4.33(m, 1H), 4.09(m, 1H), 3.33(s, 2H), 2.96(dd, 1H), 1.23(d, 3H)

Example 592

N-(2-Trifluoromethylbenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.68 (bs, 1H), 7.00-7.72(m, 13H), 5.82(d, 1H), 5.24(s, 2H), 4.80(d, 1H), 4.38(m, 1H), 4.11(m, 1H), 3.35(s, 2H), 2.99(dd, 1H), 1.22(d, 3H)

Example 593

N-(2-Trifluoromethylbenzyl)-N-(3-chloro-4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 7.01-7.72(m, 12H), 5.85(d, 1H), 5.29(s, 2H), 4.80(d, 1H), 4.42(m, 1H), 4.13(m, 1H), 3.36(s, 2H), 2.99(dd, 1H), 2.36(s, 3H), 1.24(d, 3H)

Example 594

N-(2-Trifluoromethylbenzyl)-N-cyclohexylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 7.03-7.72(m, 9H), 5.94 (bs, 1H), 5.30(s, 2H), 5.18(d, 1H), 4.88(m, 1H), 4.68(d, 1H), 4.22(m, 1H), 4.07(m, 1H), 3.33(s, 2H), 2.98(dd, 1H), 0.85-1.90(m, 10H), 1.16(d, 3H)

Example 595

N-(2-Trifluoromethylbenzyl)-N-cyclopentylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 7.03-7.71(m, 9H), 5.98 (bs, 1H), 5.34(s, 2H), 5.23(d, 1H), 4.67(d, 1H), 4.55(m, 1H), 4.07(m, 1H), 3.33(s, 2H), 2.98(dd, 1H), 1.25-1.96(m, 6H), 1.20(d, 3H)

Example 596

N-(2-Trifluoromethylbenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 7.02-7.92(m, 12H), 5.25(s, 2H), 5.20(d, 1H), 4.86(d, 1H), 4.75(m, 1H), 4.24(m, 1H), 3.32(s, 2H), 3.08(dd, 1H), 1.22(d, 3H)

Example 597

N-(2-Trifluoromethylbenzyl)-N-[2-(dimethylamino)ethylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 7.00-7.72(m, 9H), 5.40(d, 1H), 5.36(s, 2H), 4.97(m, 1H), 4.78(d, 1H), 4.21(m, 1H), 3.59(m, 2H), 3.35(d, 2H), 3.12(dd, 1H), 2.59(m, 2H), 2.03(s, 6H), 1.17(d, 3H)

Example 598

N-(2-Trifluoromethylbenzyl)-N-[4-(dimethylamino)phenylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.58-7.73(m, 13H), 5.29(s, 2H), 5.40(d, 1H),

4.86(m, 1H), 4.84(d, 1H), 4.18(m, 1H), 3.35(s, 2H), 3.04(dd, 1H), 2.96(d, 6H), 1.30(d, 3H)

Example 599

N-(2-Trifluoromethylbenzyl)-N-[3-(dimethylamino)propylthiocarbamoyl]-2(S)-
-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 7.03-7.70(m, 9H), 5.39(d, 1H), 5.24(s, 2H), 4.85(m, 1H), 4.79(d, 1H), 4.14(m, 1H), 3.74(m, 2H), 3.33 (bs, 2H), 2.95(dd, 1H), 2.63(m, 2H), 2.18(m, 2H), 1.89(s, 6H), 1.11(m, 3H)

Example 600

N-(2-Trifluoromethylbenzyl)-N-(3-ethoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.86-7.71(m, 9H), 5.35(s, 2H), 4.89(m, 1H), 4.80(dd, 2H), 4.09(m, 1H), 3.74 (bs, 2H), 3.41(m, 2H), 3.32(s, 2H), 3.15(m, 2H), 2.92(dd, 1H), 1.77 (bs, 2H), 1.12(d, 3H), 0.82 (t, 3H)

Example 601

N-(2-Trifluoromethylbenzyl)-N-ethylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 7.02-7.71(m, 9H), 6.24 (bs, 1H), 5.30(s, 2H), 5.14(d, 1H), 4.68(d, 1H), 4.58(m, 1H), 4.08(m, 1H), 3.65(m, 2H), 3.33(s, 2H), 2.94(dd, 1H), 1.27(m, 2H), 1.18(m, 3H), 1.16(d, 3H)

Example 602

N-(2-Trifluoromethylbenzyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cy

anobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.93-7.83(m, 13H), 5.36(d, 1H), 5.25(s, 2H), 4.86(d, 1H), 4.71(m, 1H), 4.21(m, 1H), 3.37(s, 2H), 3.05(dd, 1H), 1.21(d, 3H)

Example 603

N-(2-Trifluoromethylbenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.85 (bs, 1H), 6.73-7.94(m, 13H), 5.87(d, 1H), 5.27(s, 2H), 4.80(d, 1H), 4.43(m, 1H), 4.12(m, 1H), 3.36(s, 2H), 2.99(dd, 1H), 1.24(d, 3H)

Example 604

N-(2-Trifluoromethylbenzyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.66 (bs, 1H), 6.97-7.72(m, 13H), 5.79(d, 1H), 5.25(s, 2H), 4.81(d, 1H), 4.45(m, 1H), 4.12(m, 1H), 3.34(s, 2H), 2.99(dd, 1H), 1.22(d, 3H)

Example 605

N-(2-Trifluoromethylbenzyl)-N-(4-hydroxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CD_3OD) : δ 6.72-7.73(m, 13H), 5.70(d, 2H), 5.35(s, 2H), 5.05(d, 1H), 4.19(m, 1H), 3.99(m, 1H), 3.41(s, 2H), 3.25(dd, 1H), 1.18(d, 3H)

Example 606

N-(2-Trifluoromethylbenzyl)-N-(4-isopropylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.33 (bs, 1H), 6.98-7.71(m, 13H), 5.64(d, 1H), 5.25(s, 2H), 4.81(d, 1H), 4.65(m, 1H), 4.15(m, 1H), 3.33(s, 2H), 3.01(dd, 1H), 2.90(m, 1H), 1.23(m, 9H)

Example 607

N-(2-Trifluoromethylbenzyl)-N-(2-methoxyethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 7.02-7.72(m, 9H), 6.25 (bs, 1H), 5.33(s, 2H), 5.06(d, 1H), 4.86(m, 1H), 4.72(d, 1H), 4.13(m, 1H), 3.74(m, 2H), 3.42(m, 2H), 3.33(s, 2H), 3.11(s, 3H), 3.04(dd, 1H), 1.16(d, 3H)

Example 608

N-(2-Trifluoromethylbenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.21(d, 1H), 6.78-7.78(m, 13H), 5.23(s, 2H), 5.15(m, 1H), 5.09(m, 1H), 4.91(d, 1H), 4.30(m, 1H), 3.54(s, 3H), 3.35(s, 2H), 3.14(dd, 1H), 1.20(d, 3H)

Example 609

N-(2-Trifluoromethylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.30 (bs, 1H), 6.83-7.71(m, 13H), 5.63(d, 1H), 5.28(s, 2H), 4.82(d, 1H), 4.60(m, 1H), 4.14(m, 1H), 3.80(s, 3H), 3.33(s,

2H), 3.01(dd, 1H), 1.21(d, 3H)

Example 610

N-(2-Trifluoromethylbenzyl)-N-(3-methoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 7.82 (bs, 1H), 6.96-7.73(m, 9H), 5.35(d, 2H), 4.93(d, 1H), 4.70(d, 1H), 4.11(m, 1H), 3.70(m, 2H), 3.40(m, 2H), 3.32(s, 2H), 2.95(dd, 1H), 2.83(s, 3H), 1.78(m, 2H), 1.13(d, 3H)

Example 611

N-(2-Trifluoromethylbenzyl)-N-(2-methoxypyridin-5-ylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.72-8.11(m, 12H), 5.87(d, 1H), 5.25(s, 2H), 4.81(d, 1H), 4.43(m, 1H), 4.13(m, 1H), 3.92(s, 3H), 3.33(s, 2H), 2.99(dd, 1H), 1.23(d, 3H)

Example 612

N-(2-Trifluoromethylbenzyl)-N-methylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 6.98-7.70(m, 9H), 6.74(bs, 1H), 5.29(s, 2H), 5.21(d, 1H), 4.68(d, 1H), 4.51(m, 1H), 4.05(m, 1H), 3.33(s, 2H), 3.12(s, 3H), 2.91(dd, 1H), 1.16(d, 3H)

Example 613

N-(2-Trifluoromethylbenzyl)-N-(4-methylthiophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.66 (bs, 1H), 6.95-7.71(m, 13H), 5.78(d, 1H), 5.24(s, 2H), 4.801(d, 1H), 4.46(m, 1H), 4.12(m, 1H), 3.31(s, 2H), 2.98(dd, 1H), 2.47(s, 3H), 1.21(d, 3H)

Example 614

N-(2-Trifluoromethylbenzyl)-N-(2-naphthylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.99 (bs, 1H), 6.87-7.81(m, 16H), 5.84(d, 1H), 5.18(s, 2H), 4.83(d, 1H), 4.49(m, 1H), 4.16(m, 1H), 3.33(s, 2H), 2.99(dd, 1H), 1.22(d, 3H)

Example 615

N-(2-Trifluoromethylbenzyl)-N-(4-nitrophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 9.66 (bs, 1H), 6.66-8.19(m, 13H), 6.09(d, 1H), 5.25(s, 2H), 4.78(d, 1H), 4.17(m, H), 4.10(m, 1H), 3.39(s, 2H), 2.99(dd, 1H), 1.27(d, 3H)

Example 616

N-(2-Trifluoromethylbenzyl)-N-(n-pentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.70-7.72(m, 9H), 6.081 (bs, 1H), 5.33(s, 2H), 5.21(d, 1H), 4.78(m, 1H), 4.70(d, 1H), 4.10(m, 1H), 3.57(m, 1H), 3.48(s, 1H), 3.32(s, 2H), 3.02(dd, 1H), 1.60(m, 1H), 1.17(d, 3H), 0.69-1.25(m, 8H)

Example 617

N-(2-Trifluoromethylbenzyl)-N-phenethylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.99-7.64(m, 14H), 6.22 (bs, 1H), 5.30(s, 2H), 5.12(d, 1H), 4.63(m, 1H), 4.61(d, 1H), 4.02(m, 1H), 3.89(m, 2H), 3.31(s, 2H), 2.91(dd, 1H), 2.86 (t, 2H), 1.13(d, 3H)

Example 618

N-(2-Trifluoromethylbenzyl)-N-phenylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.62 (bs, 1H), 6.96-7.71(m, 14H), 5.74(d, 1H), 5.24(s, 2H), 4.81(d, 1H), 4.55(m, 1H), 4.14(m, 1H), 3.33(s, 2H), 3.00(dd, 1H), 1.21(d, 3H)

Example 619

N-(2-Trifluoromethylbenzyl)-N-(n-propylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.99-7.71(m, 9H), 6.30 (bs, 1H), 5.32(s, 2H), 5.27(d, 1H), 4.69(d, 1H), 4.64(m, 1H), 4.08(m, 1H), 3.57(m, 2H), 3.33(s, 2H), 2.96(dd, 1H), 1.53(dd, 1H), 1.17(d, 3H), 0.79 (t, 3H)

Example 620

N-(2-Trifluoromethylbenzyl)-N-(2-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.42 (bs, 1H), 6.97-7.71(m, 13H), 5.69(d, 1H), 5.25(s, 2H), 4.81(d, 1H), 4.62(m, 1H), 4.15(m, 1H), 3.34(s, 2H), 3.01(dd, 1H), 2.33(s, 3H), 1.21(d, 3H)

Example 621

N-(2-Trifluoromethylbenzyl)-N-(3-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.82 (bs, 1H), 6.97-7.73(m, 13H), 5.51(d, 1H), 5.26(s, 2H), 4.86(d, 1H), 4.75(m, 1H), 4.20(m, 1H), 3.32(s, 2H), 3.07(dd, 1H), 2.09(s, 3H), 1.21(d, 3H)

Example 622

N-(2-Trifluoromethylbenzyl)-N-(4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.39 (bs, 1H), 6.97-7.71(m, 13H), 5.66(d, 1H), 5.25(s, 2H), 4.81(d, 1H), 4.63(m, 1H), 4.15(m, 1H), 3.33(s, 2H), 3.00(dd, 1H), 2.34(s, 3H), 1.21(d, 3H)

Example 623

N-(2-Trifluoromethylbenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 9.51 (bs, 1H), 6.92-7.89(m, 13H), 6.06(d, 1H), 5.27(s, 2H), 4.78(d, 1H), 4.30(m, 1H), 4.12(m, 1H), 3.33(s, 2H), 2.97(dd, 1H), 1.25(d, 3H)

Example 624

N-(2-Trifluoromethylbenzyl)-N-(2,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.97-7.72(m, 12H), 5.46(d, 1H), 5.27(s, 2H),

4.85(d, 1H), 4.75(m, 1H), 4.19(m, 1H), 3.32(s, 2H), 3.07(dd, 1H), 2.31(s, 3H), 2.05(s, 3H), 1.20(d, 3H)

Example 625

N-(2-Trifluoromethylbenzyl)-N-(3,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminopropylamine

¹H-NMR (CDCl₃) : δ 8.30 (bs, 1H), 6.98-7.71(m, 12H), 5.64(d, 1H), 5.26(s, 2H), 4.81(d, 1H), 4.62(m, 1H), 4.15(m, 1H), 3.33(s, 2H), 3.01(dd, 1H), 2.23(s, 6H), 1.20(d, 3H)

Example 626

N-(2-Trifluoromethylbenzyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

<Step 1>

N-(2-Trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

Using the same method as described in Preparative Example 3, N-*t*-butoxycarbonyl-L-valine was converted to N-*t*-butoxycarbonyl-L-valine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 2,3-dichlorobenzylamine and 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride with 2-trifluoromethylbenzylamine and 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride, respectively, to give the title compound.

¹H-NMR (CDCl₃) : δ 7.00 - 7.65(m, 10H), 6.23(d, 1H), 5.27(s, 2H), 3.88(s, 2H), 3.81(m, 1H), 3.37(s, 2H), 2.68(d, 2H), 1.76(m, 1H), 0.84 (t,

6H)

<Step 2>

N-(2-Trifluoromethylbenzyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

To a solution of N-(2-trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added allylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 3hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: CH₂Cl₂/MeOH=9/1, v/v) to give the title compound as a white solid.

¹H-NMR (CDCl₃) : δ 7.00-7.73(m, 9H), 5.96 (bs, 1H), 5.81(m, 1H), 5.35(d, 2H), 5.02(m, 2H), 4.97(d, 1H), 4.65(d, 1H), 4.26(m, 1H), 4.04(m, 1H), 3.33(s, 2H), 3.08(dd, 1H), 1.87(m, 1H), 0.91 (t, 6H)

Examples 627-669

N-(2-Trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 626 to give the title compounds.

Example 627

N-(2-Trifluoromethylbenzyl)-N-benzylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 6.99-7.68(m, 14H), 6.21 (bs, 1H), 5.27(d, 2H),

5.05 (t, 1H), 4.96(d, 1H), 4.81(dd, 2H), 4.67(d, 1H), 4.05(m, 1H), 3.28(s, 2H), 3.10(dd, 1H), 1.83(m, 1H), 1.90(dd, 6H)

Example 628

N-(2-Trifluoromethylbenzyl)-N-(2-biphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 6.89-7.71(m, 18H), 5.25(s, 2H), 5.20(m, 1H), 4.76(m, 1H), 4.62(d, 1H), 3.97(m, 1H), 3.33(s, 2H), 2.99(dd, 1H), 1.84(m, 1H), 0.85(dd, 6H)

Example 629

N-(2-Trifluoromethylbenzyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 7.02-7.76(m, 13H), 5.26(s, 2H), 5.20(d, 1H), 5.17(m, 1H), 4.88(d, 1H), 4.39(m, 1H), 3.38(s, 2H), 3.20(dd, 1H), 1.88(m, 1H), 0.91(dd, 6H)

Example 630

N-(2-Trifluoromethylbenzyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 8.47 (bs, 1H), 6.795-7.72(m, 13H), 5.54(d, 1H), 5.27(s, 2H), 4.76(d, 1H), 4.72(m, 1H), 4.05(m, 1H), 3.35(s, 2H), 3.14(dd, 1H), 1.90(m, 1H), 0.90 (t, 6H)

Example 631

N-(2-Trifluoromethylbenzyl)-N-(4-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 8.28 (bs, 1H), 6.80-7.74(m, 13H), 5.47(d, 1H), 5.28(d, 2H), 4.79(m, 1H), 4.78(d, 1H), 4.07(m, 1H), 3.36(s, 2H), 3.16(dd, 1H), 1.91(m, 1H), 0.91(m, 6H)

Example 632

N-(2-Trifluoromethylbenzyl)-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.01-7.73(m, 9H), 5.71 (bs, 1H), 5.35(d, 2H), 5.05 (t, 1H), 4.75(dd, 2H), 4.02(m, 1H), 3.53(m, 2H), 3.33(s, 2H), 3.07(dd, 1H), 1.87(m, 1H), 1.40(m, 2H), 1.07(m, 2H), 0.91(dd, 6H), 0.80 (t, 3H)

Example 633

N-(2-Trifluoromethylbenzyl)-N-isobutylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.02-7.74(m, 9H), 5.69 (bs, 1H), 5.37(d, 2H), 5.14 (t, 1H), 4.76(dd, 2H), 4.05(m, 1H), 3.48(m, 1H), 3.34(s, 2H), 3.28(m, 1H), 3.12(dd, 1H), 1.87(m, 1H), 1.76(m, 1H), 0.93(dd, 6H), 0.70(m, 6H)

Example 634

N-(2-Trifluoromethylbenzyl)-N-(2-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.96-7.76(m, 13H), 5.28(d, 2H), 5.17(d, 1H), 5.09(m, 1H), 4.87(d, 1H), 4.19(m, 1H), 3.38(d, 2H), 3.19(dd, 1H), 1.90(m, 1H), 0.92 (t, 6H)

Example 635

N-(2-Trifluoromethylbenzyl)-N-(3-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 8.45 (bs, 1H), 6.82-7.74(m, 13H), 5.55(d, 1H), 5.29(d, 2H), 4.78 (d 1H), 4.74(m, 1H), 4.07(m, 1H), 3.37(s, 2H), 3.16(dd, 1H), 1.92(m, 1H), 0.92 (t, 6H)

Example 636

N-(2-Trifluoromethylbenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 8.26 (bs, 1H), 6.81-7.73(m, 13H), 5.46(d, 1H), 5.25(d, 2H), 4.80(m, 1H), 4.77(d, 1H), 4.05(m, 1H), 3.35(s, 2H), 3.14(dd, 1H), 1.90(m, 1H), 0.90 (t, 6H)

Example 637

N-(2-Trifluoromethylbenzyl)-N-(3-chloro-4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 8.29 (bs, 1H), 6.87-7.73(m, 12H), 5.49(d, 1H), 5.28(s, 2H), 4.79(m, 1H), 4.77(d, 1H), 4.07(m, 1H), 3.36(s, 2H), 3.14(dd, 1H), 2.34(s, 3H), 1.91(m, 1H), 0.91 (t, 6H)

Example 638

N-(2-Trifluoromethylbenzyl)-N-cyclohexylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 7.04-7.74(m, 9H), 5.98 (bs, 1H), 5.36(s, 2H), 5.12

(t, 1H), 4.75(dd, 1H), 4.18(m, 1H), 4.01(m, 1H), 3.34(s, 2H), 3.08(dd, 1H), 1.84(m, 1H), 0.83-1.98(m, 10H), 0.90 (t, 6H)

Example 639

N-(2-Trifluoromethylbenzyl)-N-cyclopentylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR (CDCl₃) : δ 7.03-7.73(m, 9H), 5.54 (bs, 1H), 5.35(d, 2H), 5.03 (t, 1H), 4.75(dd, 2H), 4.61(m, 1H), 4.01(m, 1H), 3.34(s, 2H), 3.08(dd, 1H), 1.85(m, 1H), 1.09-2.06(m, 8H), 0.91(dd, 6H)

Example 640

N-(2-Trifluoromethylbenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 6.82-7.75(m, 12H), 5.28(d, 1H), 5.26(s, 2H), 4.92(m, 1H), 4.85(d, 1H), 4.16(m, 1H), 3.35(s, 2H), 3.19(dd, 1H), 1.87(m, 1H), 0.90(t, 6H)

Example 641

N-(2-Trifluoromethylbenzyl)-N-[2-(dimethylamino)ethylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 7.02-7.71(m, 9H), 6.82(bs, 1H), 5.36(dd, 2H), 4.79(m, 3H), 4.28(m, 1H), 3.56(m, 2H), 3.33(d, 2H), 3.14(dd, 1H), 2.44(m, 2H), 1.97(s, 6H), 1.88(m, 1H), 0.89(d, 6H)

Example 642

N-(2-Trifluoromethylbenzyl)-N-[4-(dimethylamino)phenylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.61-7.73(m, 13H), 5.29(s, 2H), 5.18(d, 1H), 5.14(m, 1H), 4.79(d, 1H), 4.08(m, 1H), 3.35(s, 2H), 3.12(dd, 1H), 2.93(s, 6H), 1.88(m, 1H), 0.90(dd, 6H)

Example 643

N-(2-Trifluoromethylbenzyl)-N-[3-(dimethylamino)propylthiocarbamoyl]-2(S)-
-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.87(bs, 1H), 7.04-7.72(m, 13H), 5.41(dd, 2H), 4.92(m, 1H), 4.74(s, 2H), 4.01(m, 1H), 3.73(m, 2H), 3.35(d, 2H), 2.92(dd, 1H), 2.44(m, 2H), 1.89(s, 6H), 1.83(m, 1H), 1.80(m, 2H), 0.88(dd, 6H)

Example 644

N-(2-Trifluoromethylbenzyl)-N-(3-ethoxypropylthiocarbamoyl)-2(S)-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.04-7.72(m, 9H), 6.75(bs, 1H), 5.38(dd, 2H), 5.09(t, 1H), 4.70(dd, 2H), 4.01(m, 1H), 3.75(m, 2H), 3.39(m, 2H), 3.36(s, 2H), 3.14(m, 2H), 2.95(dd, 1H), 1.85(m, 1H), 1.81(m, 2H), 0.88(dd, 6H), 0.80(t, 3H)

Example 645

N-(2-Trifluoromethylbenzyl)-N-ethylthiocarbamoyl-2(S)-[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.00-7.72(m, 9H), 5.80(bs, 1H), 5.35(dd, 2H), 4.98(t, 1H), 4.93(d, 1H), 4.62(d, 1H), 4.02(m, 1H), 3.60(m, 2H), 3.33(s, 2H), 3.05(dd, 1H), 1.87(m, 1H), 1.06(t, 3H), 0.90(m, 6H)

Example 646

N-(2-Trifluoromethylbenzyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.93-7.75(m, 13H), 5.29(d, 1H), 5.27(s, 2H), 5.01(t, 1H), 4.83(d, 1H), 4.13(m, 1H), 3.37(s, 2H), 3.151(dd, 1H), 1.88(m, 1H), 0.90(t, 6H)

Example 647

N-(2-Trifluoromethylbenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.35(bs, 1H), 6.82-7.73(m, 13H), 5.50(d, 1H), 5.27(s, 2H), 4.80(m, 1H), 4.77(d, 1H), 4.06(m, 1H), 3.36(s, 2H), 3.15(dd, 1H), 1.89(m, 1H), 0.91(t, 6H)

Example 648

N-(2-Trifluoromethylbenzyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.05(bs, 1H), 6.87-7.73(m, 13H), 5.38(d, 1H), 5.27(s, 2H), 4.82(m, 1H), 4.78(d, 1H), 4.06(m, 1H), 3.34(s, 2H), 3.15(dd, 1H), 1.88(m, 1H), 0.90(t, 6H)

Example 649

N-(2-Trifluoromethylbenzyl)-N-(4-hydroxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CD}_3\text{OD})$: δ 6.69-7.75(m, 13H), 5.43(d, 1H), 5.37(s, 2H),

5.05(d, 1H), 4.25(m, 2H), 3.49(dd, 2H), 2.68(m, 1H), 1.77(m, 1H), 0.90(d, 6H)

Example 650

N-(2-Trifluoromethylbenzyl)-N-(4-isopropylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 7.02-7.73(m, 13H), 5.27(s, 2H), 5.18(d, 1H), 5.04(t, 1H), 4.79(d, 1H), 4.08(m, 1H), 3.35(s, 2H), 3.14(dd, 1H), 2.89(m, 1H), 1.87(m, 1H), 1.22(d, 6H), 0.91(t, 6H)

Example 651

N-(2-Trifluoromethylbenzyl)-N-(2-methoxyethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 7.03-7.73(m, 9H), 5.96(bs, 1H), 5.36(dd, 2H), 5.11(t, 1H), 4.73(dd, 1H), 4.13(m, 1H), 3.70(m, 2H), 3.37(m, 2H), 3.34(s, 2H), 3.09(dd, 1H), 3.07(s, 3H), 1.86(m, 1H), 0.91(d, 6H)

Example 652

N-(2-Trifluoromethylbenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 8.28(d, 1H), 6.76-7.78(m, 13H), 5.20(s, 2H), 5.19(t, 1H), 5.01(dd, 2H), 4.18(m, 1H), 3.52(s, 3H), 3.37(s, 2H), 3.15(dd, 1H), 1.87(m, 1H), 0.94(d, 6H)

Example 653

N-(2-Trifluoromethylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.82-7.73(m, 13H), 5.30(s, 2H), 5.25(d, 1H), 4.99(s, 1H), 4.79(d, 1H), 4.07(m, 1H), 3.78(s, 3H), 3.35(s, 2H), 3.13(dd, 1H), 1.88(m, 1H), 0.90(t, 6H)

Example 654

N-(2-Trifluoromethylbenzyl)-N-(3-methoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.81-7.73(m, 9H), 5.38(dd, 2H), 5.11(t, 1H), 4.68(s, 2H), 4.02(m, 1H), 3.70(m, 2H), 3.39(m, 2H), 3.33(s, 2H), 2.97(dd, 1H), 2.80(s, 3H), 1.83(m, 1H), 1.77(m, 2H), 0.89(d, 6H)

Example 655

N-(2-Trifluoromethylbenzyl)-N-(2-methoxypyridin-5-ylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.28(bs, 1H), 6.69-7.91(m, 12H), 5.45(d, 1H), 5.27(d, 2H), 4.81(m, 1H), 4.78(d, 1H), 4.07(m, 1H), 3.90(s, 3H), 3.33(s, 2H), 3.14(dd, 1H), 1.91(m, 1H), 0.90(t, 6H)

Example 656

N-(2-Trifluoromethylbenzyl)-N-methylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.97-7.71(m, 9H), 6.20(bs, 1H), 5.35(dd, 2H), 4.96(d, 1H), 4.91(t, 1H), 4.61(d, 1H), 4.00(m, 1H), 3.33(s, 2H), 3.08(s, 3H), 3.04(dd, 1H), 1.86(m, 1H), 0.90(t, 6H)

Example 657

N-(2-Trifluoromethylbenzyl)-N-(4-methylthiophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.94(bs, 1H), 6.88-7.73(m, 13H), 5.36(d, 1H), 5.26(d, 2H), 4.92(t, 1H), 4.78(d, 1H), 4.06(m, 1H), 3.35(s, 2H), 3.14(dd, 1H), 2.46(s, 3H), 1.88(m, 1H), 0.90(t, 6H)

Example 658

N-(2-Trifluoromethylbenzyl)-N-(2-naphthylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.21(bs, 1H), 6.85-7.82(m, 16H), 5.44(d, 1H), 5.20(d, 2H), 4.97(m, 1H), 4.83(d, 1H), 4.11(m, 1H), 3.37(s, 2H), 3.16(dd, 1H), 1.89(m, 1H), 0.91(t, 6H)

Example 659

N-(2-Trifluoromethylbenzyl)-N-(4-nitrophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 9.13(bs, 1H), 6.62-8.17(m, 13H), 5.73(d, 1H), 5.26(s, 2H), 4.76(d, 1H), 4.56(m, 1H), 4.03(m, 1H), 3.38(s, 2H), 3.19(dd, 1H), 1.96(m, 1H), 0.91(dd, 6H)

Example 660

N-(2-Trifluoromethylbenzyl)-N-(n-pentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.02-7.74(m, 9H), 5.59(bs, 1H), 5.36(dd, 2H), 5.17(t, 1H), 4.74(dd, 2H), 4.04(m, 1H), 3.33(s, 2H), 3.19-3.74(m, 2H), 3.11(dd, 1H), 1.87(m, 1H), 1.51(m, 1H), 1.14(m, 1H), 1.06(m, 2H),

0.92(dd, 6H), 0.87(m, 2H), 0.64(t, 3H)

Example 661

N-(2-Trifluoromethylbenzyl)-N-phenethylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 6.97-7.68(m, 14H), 5.70(bs, 1H), 5.34(dd, 2H), 4.99(t, 1H), 4.64(dd, 2H), 3.99(m, 1H), 3.86(m, 2H), 3.32(s, 2H), 3.01(dd, 1H), 2.80(t, 2H), 1.83(m, 1H), 0.89(dd, 6H)

Example 662

N-(2-Trifluoromethylbenzyl)-N-phenylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 7.94(bs, 1H), 6.94-7.73(m, 14H), 5.36(d, 1H), 5.26(s, 2H), 4.98(t, 1H), 4.80(d, 1H), 4.08(m, 1H), 3.35(s, 2H), 3.14(dd, 1H), 1.87(m, 1H), 0.90(dd, 6H)

Example 663

N-(2-Trifluoromethylbenzyl)-N-(n-propylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 7.00-7.72(m, 9H), 5.74(bs, 1H), 5.35(dd, 2H), 5.05(t, 1H), 4.76(dd, 2H), 4.02(m, 1H), 3.58(m, 1H), 3.48(m, 1H), 3.33(s, 2H), 3.07(dd, 1H), 1.85(m, 1H), 1.45(m, 2H), 0.91(dd, 6H), 0.72(t, 3H)

Example 664

N-(2-Trifluoromethylbenzyl)-N-(2-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.94-7.75(m, 13H), 5.35(d, 1H), 5.28(s, 2H), 5.00(t, 1H), 5.02(t, 1H), 4.81(d, 1H), 4.10(m, 1H), 3.37(s, 2H), 3.15(dd, 1H), 2.33(s, 3H), 1.89(m, 1H), 0.92(dd, 6H)

Example 665

N-(2-Trifluoromethylbenzyl)-N-(3-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.01-7.75(m, 13H), 5.30(s, 2H), 5.23(d, 1H), 5.10(t, 1H), 4.84(d, 1H), 4.14(m, 1H), 3.36(s, 2H), 3.18(dd, 1H), 2.01(s, 3H), 1.91(m, 1H), 0.91(t, 6H)

Example 666

N-(2-Trifluoromethylbenzyl)-N-(4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.76(bs, 1H), 7.00-7.73(m, 13H), 5.27(s, 2H), 5.23(d, 1H), 5.00(t, 1H), 4.79(d, 1H), 4.08(m, 1H), 3.35(s, 2H), 3.13(dd, 1H), 2.32(s, 3H), 1.87(m, 1H), 0.90(t, 6H)

Example 667

N-(2-Trifluoromethylbenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.82(bs, 1H), 6.75-7.73(m, 13H), 5.67(d, 1H), 5.26(s, 2H), 4.77(d, 1H), 4.62(m, 1H), 4.06(m, 1H), 3.36(s, 2H), 3.17(dd, 1H), 1.92(m, 1H), 0.91(t, 6H)

Example 668

N-(2-Trifluoromethylbenzyl)-N-(2,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(

4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 6.92-7.75(m, 13H), 5.29(s, 2H), 5.21(d, 1H), 5.15(m, 1H), 4.83(d, 1H), 4.12(m, 1H), 3.35(s, 2H), 3.17(dd, 1H), 2.30(s, 3H), 1.96(s, 3H), 1.90(m, 1H), 0.90(t, 6H)

Example 669

N-(2-Trifluoromethylbenzyl)-N-(3,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-methylbutylamine

¹H-NMR(CDCl₃) : δ 6.93-7.73(m, 13H), 5.28(s, 2H), 5.22(d, 1H), 5.02(t, 1H), 4.79(d, 1H), 4.10(m, 1H), 3.36(s, 2H), 3.13(dd, 1H), 2.21(s, 6H), 1.86(m, 1H), 0.90(t, 6H)

Example 670

N-(2-Trifluoromethylbenzyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

<Step 1>

N-(2-Trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

Using the same method as described in Preparative Example 3, N-*t*-butoxycarbonyl-L-leucine was converted to N-*t*-butoxycarbonyl-L-leucine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 2,3-dichlorobenzylamine and 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride with 2-trifluoromethylbenzylamine and 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride, respectively, to give the title compound.

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.00-7.66(m, 10H), 6.14(d, 1H), 5.27(s, 2H), 4.08(m, 1H), 3.90(s, 2H), 3.35(s, 2H), 2.65(d, 2H), 1.52(m, 1H), 1.27(m, 2H), 0.88(d, 6H)

<Step 2>

N-(2-Trifluoromethylbenzyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

To a solution of N-(2-trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added allylisothiocyanate (0.1M in CH_2Cl_2 , 0.2ml, 0.02mmol). The reaction mixture was agitated for 3hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: $\text{CH}_2\text{Cl}_2/\text{MeOH}=9/1$, v/v) to give the title compound as a white solid.

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.78-7.71(m, 11H), 6.40(bs, 1H), 5.85(m, 2H), 5.33(d, 2H), 4.69-5.07(dd, 2H), 4.69(bs, 1H), 4.33(d, 2H), 4.15(m, 1H), 3.31(s, 2H), 3.05(dd, 1H), 1.25-1.52(m, 3H), 0.85(d, 6H)

Examples 671-713

N-(2-Trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 670 to give the title compounds.

Example 671

N-(2-Trifluoromethylbenzyl)-N-benzylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl

)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 6.72-7.67(m, 14H), 6.75(bs, 1H), 5.22(d, 2H), 4.63-4.98(m, 3H), 4.17(m, 1H), 3.25(s, 2H), 3.05(dd, 1H), 1.25-1.62(m, 3H), 0.85(d, 6H)

Example 672

N-(2-Trifluoromethylbenzyl)-N-(2-biphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 6.93-7.71(m, 19H), 6.66(bs, 1H), 5.12-5.21(m, 3H), 4.67-4.76(d, 1H), 4.09(m, 1H), 3.29(s, 2H), 2.92(dd, 1H), 1.10-1.62(m, 3H), 0.83(d, 6H)

Example 673

N-(2-Trifluoromethylbenzyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 6.99-7.82(m, 13H), 6.65(bs, 1H), 5.48(m, 1H), 5.29(s, 1H), 5.22(s, 2H), 4.87-4.96(d, 1H), 4.71(m, 1H), 4.36(m, 1H), 3.35(s, 2H), 3.14(dd, 1H), 1.25-1.62(m, 3H), 0.89(d, 6H)

Example 674

N-(2-Trifluoromethylbenzyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 8.95(bs, 1H), 6.96-7.71(m, 13H), 6.66(d, 1H), 5.75(bd, 1H), 5.26(s, 2H), 4.86(d, 1H), 4.40(m, 1H), 4.13(m, 1H), 3.34(s, 2H), 3.03(dd, 1H), 1.26-1.70(m, 3H), 0.86(d, 6H)

Example 675

N-(2-Trifluoromethylbenzyl)-N-(4-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.73(bs, 1H), 6.95-7.71(13H), 6.63(d, 1H), 5.70(d, 1H), 5.21(s, 2H), 4.85(d, 1H), 4.47(m, 1H), 4.14(m, 1H), 3.34(s, 2H), 3.03(dd, 1H), 1.26-1.70(m, 3H), 0.86(d, 6H)

Example 676

N-(2-Trifluoromethylbenzyl)-N-(n-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.98-7.82(m, 9H), 6.86(d, 1H), 6.22(bs, 1H), 5.00-5.42(m, 3H), 4.70(d, 1H), 4.14(m, 1H), 3.40-3.78(m, 2H), 3.32(s, 2H), 2.99(dd, 1H), 1.11-1.70(m, 8H), 0.88(m, 10H)

Example 677

N-(2-Trifluoromethylbenzyl)-N-isobutylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.86-7.82(m, 10H), 6.11(bs, 1H), 4.98-5.52(m, 3H), 4.66-4.75(d, 2H), 4.18(bs, 1H), 3.47-3.80(m, 1H), 3.31(s, 2H), 3.03(dd, 1H), 1.75-1.96(m, 2H), 1.21-1.68(m, 3H), 0.89(d, 6H), 0.75(d, 6H)

Example 678

N-(2-Trifluoromethylbenzyl)-N-(2-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.98-7.74(m, 13H), 6.66(bs, 1H), 5.38-5.60(bs, 1H), 5.22(s, 2H), 4.90(d, 1H), 4.70(m, 1H), 4.35(m, 1H), 3.35(s, 2H), 3.12(dd,

1H), 1.25-1.60(m, 3H), 0.89(d, 6H)

Example 679

N-(2-Trifluoromethylbenzyl)-N-(3-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 8.93(bs, 1H), 6.95-7.71(13H), 6.70(d, 1H), 5.75(bd, 1H), 5.25(s, 2H), 4.90(d, 1H), 4.39 9m, 1H), 4.15(m, 1H), 3.34(s, 2H), 3.02(dd, 1H), 1.25-1.68(m, 3H), 0.86(d, 6H)

Example 680

N-(2-Trifluoromethylbenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 8.71(1H, br), 6.95-7.71(m, 13H), 6.63(d, 1H), 5.70(bd, 1H), 5.22(s, 2H), 4.46(m, 1H), 4.16(m, 1H), 3.34(s, 2H), 3.04(dd, 1H), 1.25-1.70(m, 3H), 0.86(d, 6H)

Example 681

N-(2-Trifluoromethylbenzyl)-N-(3-chloro-4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 8.71(bs, 1H), 6.96-7.71(m, 2H), 6.70(d, 1H), 5.70(bd, 1H), 5.25(s, 2H), 4.88(d, 1H), 4.30(m, 1H), 4.15(m, 1H), 3.34(s, 2H), 3.03(dd, 1H), 2.34(s, 3H), 1.26-1.70(m, 3H), 0.86(d, 6H)

Example 682

N-(2-Trifluoromethylbenzyl)-N-cyclohexylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.96-7.72(m, 9H), 6.86(bd, 1H), 5.86(bs, 1H), 5.10-5.30(m, 3H), 4.70(d, 2H), 4.20(m, 2H), 3.32(s, 2H), 3.03(dd, 1H), 1.72-2.10(m, 3H), 1.20-1.70(m, 8H), 0.86(d, 6H)

Example 683

N-(2-Trifluoromethylbenzyl)-N-cyclopentylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.96-7.72(m, 9H), 6.85(bd, 1H), 5.95(bs, 1H), 5.10-5.42(m, 3H), 4.66(m, 2H), 4.15(m, 1H), 3.32(s, 2H), 3.03(dd, 1H), 1.80-2.10(m, 3H), 1.10-1.72(m, 9H), 0.86(d, 6H)

Example 684

N-(2-Trifluoromethylbenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.98-7.73(m, 12H), 6.55(bd, 1H), 5.52(m, 1H), 5.22(s, 2H), 4.90(d, 1H), 4.59(m, 1H), 4.32(m, 1H), 3.34(s, 2H), 3.10(dd, 1H), 1.25-1.62(m, 3H), 0.87(d, 6H)

Example 685

N-(2-Trifluoromethylbenzyl)-N-[2-(dimethylamino)ethylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.03-7.72(m, 10H), 6.72(bs, 1H), 5.39(dd, 2H), 5.07(m, 1H), 4.74(m, 2H), 4.08(m, 1H), 3.52(bs, 2H), 3.36(s, 2H), 3.13(dd, 1H), 2.45(m, 2H), 2.32(bs, 2H), 1.91(s, 6H), 0.92(d, 6H)

Example 686

N-(2-Trifluoromethylbenzyl)-N-[4-(dimethylamino)phenylthiocarbamoyl]-2(S)

-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.83(bs, 1H), 6.58-7.72(m, 14H), 5.38(d, 1H), 5.26(s, 2H), 4.86(d, 1H), 4.74(m, 1H), 4.24(m, 1H), 3.34(s, 2H), 3.07(dd, 1H), 2.94(s, 6H), 1.26-1.57(m, 3H), 0.88(d, 6H)

Example 687

N-(2-Trifluoromethylbenzyl)-N-[3-(dimethylamino)propylthiocarbamoyl]-2(S)-
-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.75(bs, 1H), 7.02-7.71(m, 10H), 5.38(dd, 2H), 4.82(m, 3H), 4.24(m, 1H), 3.71(m, 2H), 3.32(dd, 2H), 2.94(dd, 1H), 2.55(m, 4H), 2.02(bs, 6H), 1.49(m, 2H), 1.19(m, 1H), 0.86(d, 6H)

Example 688

N-(2-Trifluoromethylbenzyl)-N-(3-ethoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.03-7.71(m, 10H), 6.87(bs, 1H), 5.35(dd, 2H), 4.80(m, 3H), 4.20(m, 1H), 3.75(m, 2H), 3.41(m, 2H), 3.31(s, 2H), 3.16(m, 2H), 2.95(dd, 1H), 1.80(m, 2H), 1.17-1.54(m, 3H), 0.85(m, 9H)

Example 689

N-(2-Trifluoromethylbenzyl)-N-ethylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.78-7.71(m, 10H), 6.28(bs, 1H), 5.32(d, 2H), 5.22(d, 1H), 4.70(d, 1H), 4.60(m, 1H), 3.64(m, 2H), 3.32(s, 2H), 2.99(dd, 1H), 2.94(s, 6H), 1.26-1.57(m, 3H), 1.11(t, 3H), 0.87(m, 6H)

Example 690

N-(2-Trifluoromethylbenzyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.12(bs, 1H), 6.69-7.72(m, 14H), 5.52(d, 1H), 5.23(s, 2H), 4.90(d, 1H), 4.66(m, 1H), 4.30(m, 1H), 3.08(dd, 1H), 1.26-1.58(m, 3H), 0.88(d, 6H)

Example 691

N-(2-Trifluoromethylbenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.85(bs, 1H), 6.69-7.71(m, 14H), 5.81(q, 1H), 5.24(s, 2H), 4.88(d, 1H), 4.49(m, 1H), 4.07(m, 1H), 3.34(d, 2H), 3.04(dd, 1H), 1.21-1.60(m, 3H), 0.88(d, 6H)

Example 692

N-(2-Trifluoromethylbenzyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.52(bs, 1H), 6.65-7.71(m, 14H), 5.62(d, 1H), 5.23(s, 2H), 4.88(d, 1H), 4.51(m, 1H), 4.17(m, 1H), 3.34(d, 2H), 3.05(dd, 1H), 1.26-1.58(m, 3H), 0.87(dd, 6H)

Example 693

N-(2-Trifluoromethylbenzyl)-N-(4-hydroxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.18(bs, 1H), 6.69-7.70(m, 14H), 5.38(d, 1H), 5.23(d, 2H), 4.86(d, 1H), 4.78(m, 1H), 4.23(m, 1H), 3.33(s, 2H), 3.04(dd,

1H), 1.26-1.58(m, 3H), 0.87(d, 6H)

Example 694

N-(2-Trifluoromethylbenzyl)-N-(4-isopropylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 8.20(bs, 1H), 6.74-7.71(m, 14H), 5.51(d, 1H), 5.23(s, 2H), 4.87(d, 1H), 4.69(m, 1H), 4.20(m, 1H), 3.34(s, 2H), 3.07(dd, 1H), 2.90(m, 1H), 1.23(d, 6H), 1.14-1.58(m, 3H), 0.89(m, 6H)

Example 695

N-(2-Trifluoromethylbenzyl)-N-(2-methoxyethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 6.92-7.72(m, 10H), 6.24(bs, 1H), 5.33(dd, 2H), 4.86(dd, 2H), 4.78(m, 1H), 4.23(m, 1H), 3.73(m, 2H), 3.39(m, 2H), 3.32(s, 2H), 3.10(s, 3H), 3.08(dd, 1H), 1.26-1.58(m, 3H), 0.89(d, 6H)

Example 696

N-(2-Trifluoromethylbenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 6.77-8.26(m, 14H), 5.19(s, 2H), 5.06(m, 1H), 5.03(dd, 2H), 4.39(m, 1H), 3.54(s, 3H), 3.36(s, 2H), 3.16(dd, 1H), 1.26-1.62(m, 3H), 0.92(d, 6H)

Example 697

N-(2-Trifluoromethylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.20(bs, 1H), 6.78-7.72(m, 14H), 5.51(d, 1H), 5.24(m, 1H), 4.87(d, 1H), 4.65(m, 1H), 4.23(m, 1H), 3.79(s, 3H), 3.33(s, 2H), 3.06(dd, 1H), 1.26-1.58(m, 3H), 0.87(d, 6H)

Example 698

N-(2-Trifluoromethylbenzyl)-N-(3-methoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.02-7.73(m, 10H), 6.91(bs, 1H), 5.35(d, 2H), 4.85(m, 1H), 4.78(dd, 2H), 4.21(m, 1H), 3.70(m, 2H), 3.39(m, 2H), 3.40(m, 2H), 3.31(s, 2H), 2.98(dd, 1H), 2.83(s, 3H), 1.77(m, 2H), 1.18-1.56(m, 3H), 0.87(d, 6H)

Example 699

N-(2-Trifluoromethylbenzyl)-N-(2-methoxypyridin-5-ylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.75(bs, 1H), 6.69-7.99(m, 13H), 5.69(d, 1H), 5.24(s, 2H), 4.88(d, 1H), 4.49(m, 1H), 4.18(m, 1H), 3.91(s, 3H), 3.33(s, 2H), 3.05(dd, 1H), 1.26-1.58(m, 3H), 0.87(dd, 6H)

Example 700

N-(2-Trifluoromethylbenzyl)-N-methylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.21(bs, 1H), 6.69-7.72(m, 10H), 5.53(d, 1H), 5.23(s, 2H), 4.87(d, 1H), 4.66(m, 1H), 4.24(m, 1H), 3.35(s, 2H), 3.06(dd, 1H), 2.32(s, 3H), 1.26-1.58(m, 3H), 0.88(d, 6H)

Example 701

N-(2-Trifluoromethylbenzyl)-N-(4-methylthiophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.51(bs, 1H), 6.72-7.71(m, 14H), 5.62(d, 1H), 5.22(s, 2H), 4.87(d, 1H), 4.56(m, 1H), 4.20(m, 1H), 3.34(s, 2H), 3.05(dd, 1H), 2.47(s, 3H), 1.26-1.58(m, 3H), 0.88(dd, 6H)

Example 702

N-(2-Trifluoromethylbenzyl)-N-(2-naphthylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.73(bs, 1H), 6.72-7.80(m, 17H), 5.69(d, 1H), 5.16(s, 2H), 4.91(d, 1H), 4.61(m, 1H), 4.24(m, 1H), 3.35(s, 2H), 3.07(dd, 1H), 1.26-1.58(m, 3H), 0.88(dd, 6H)

Example 703

N-(2-Trifluoromethylbenzyl)-N-(4-nitrophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 9.51(bs, 1H), 6.64-8.18(m, 14H), 5.89(d, 1H), 5.23(s, 2H), 4.90(d, 1H), 4.26(m, 1H), 4.11(m, 1H), 3.39(s, 2H), 3.07(dd, 1H), 1.26-1.53(m, 3H), 0.86(t, 6H)

Example 704

N-(2-Trifluoromethylbenzyl)-N-(n-pentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.88-7.72(m, 10H), 6.01(bs, 1H), 5.24(m, 3H), 4.78(m, 1H), 4.71(d, 1H), 4.20(m, 1H), 3.61(m, 1H), 3.48(m, 1H), 3.32(s, 2H), 3.06(dd, 1H), 0.68-1.60(m, 12H), 0.90(d, 6H)

Example 705

N-(2-Trifluoromethylbenzyl)-N-phenethylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 6.99-7.67(m, 14H), 6.88(bs, 1H), 5.30(d, 2H), 4.98(d, 1H), 4.63(d, 1H), 4.62(m, 1H), 4.14(m, 1H), 3.88(m, 2H), 3.30(s, 2H), 2.97(dd, 1H), 2.84(t, 2H), 1.22-1.54(m, 3H), 0.86(dd, 6H)

Example 706

N-(2-Trifluoromethylbenzyl)-N-phenylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 8.27(bs, 1H), 6.64-7.72(m, 15H), 5.54(d, 1H), 5.23(s, 2H), 4.88(d, 1H), 4.66(m, 1H), 4.23(m, 1H), 3.34(s, 2H), 3.07(dd, 1H), 2.84(t, 2H), 1.26-1.59(m, 3H), 0.87(dd, 6H)

Example 707

N-(2-Trifluoromethylbenzyl)-N-(n-propylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 6.82-7.71(m, 10H), 6.23(bs, 1H), 5.32(d, 2H), 5.17(d, 1H), 4.70(d, 1H), 4.64(m, 1H), 4.16(m, 1H), 3.58(m, 2H), 3.32(s, 2H), 3.01(dd, 1H), 1.51(m, 2H), 1.26-1.60(m, 3H), 0.88(m, 6H), 0.77(t, 3H)

Example 708

N-(2-Trifluoromethylbenzyl)-N-(2-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.21(bs, 1H), 6.69-7.72(m, 14H), 5.53(d, 1H), 5.23(s, 2H), 4.87(d, 1H), 4.66(m, 1H), 4.24(m, 1H), 3.35(s, 2H), 3.06(dd, 1H), 2.32(s, 3H), 1.26-1.58(m, 3H), 0.88(d, 6H)

Example 709

N-(2-Trifluoromethylbenzyl)-N-(3-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 6.69-7.72(m, 10H), 5.47(d, 1H), 5.24(s, 2H), 4.89(d, 1H), 4.73(m, 1H), 4.28(m, 1H), 3.34(s, 2H), 3.11(dd, 1H), 2.08(s, 3H), 1.26-1.60(m, 3H), 0.89(d, 6H)

Example 710

N-(2-Trifluoromethylbenzyl)-N-(4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.24(bs, 1H), 6.74-7.72(m, 14H), 5.53(d, 1H), 5.24(s, 2H), 4.88(d, 1H), 4.68(m, 1H), 4.24(m, 1H), 3.34(s, 2H), 3.07(dd, 1H), 2.34(s, 3H), 1.26-1.58(m, 3H), 0.88(d, 6H)

Example 711

N-(2-Trifluoromethylbenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 9.26(bs, 1H), 6.64-7.83(m, 14H), 5.85(d, 1H), 5.24(s, 2H), 4.90(d, 1H), 4.34(m, 1H), 4.13(m, 1H), 3.34(s, 2H), 3.04(dd, 1H), 2.32(s, 3H), 1.26-1.58(m, 3H), 0.86(t, 6H)

Example 712

N-(2-Trifluoromethylbenzyl)-N-(2,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(

4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 6.82-7.73(m, 13H), 5.37(d, 1H), 5.25(s, 2H), 4.88(d, 1H), 4.72(m, 1H), 4.28(m, 1H), 3.34(s, 2H), 3.10(dd, 1H), 2.31(s, 3H), 2.03(s, 3H), 1.26-1.58(m, 3H), 0.88(d, 6H)

Example 713

N-(2-Trifluoromethylbenzyl)-N-(3,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-4-methylpentylamine

¹H-NMR(CDCl₃) : δ 8.11(bs, 1H), 6.75-7.72(m, 13H), 5.49(d, 1H), 5.24(s, 2H), 4.87(d, 1H), 4.67(m, 1H), 4.24(m, 1H), 3.35(s, 2H), 3.06(dd, 1H), 2.22(s, 6H), 1.26-1.58(m, 3H), 0.88(d, 6H)

Example 714

N-(2-Trifluoromethylbenzyl)-N-allylthiocarbamoyl-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

<Step 1>

N-(2-Trifluoromethylbenzyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

Using the same methods as described in Preparative Example 3, 2-(N-*t*-butoxycarbonylamino)-2-methylpropionic acid was converted to 2-(N-*t*-butoxycarbonylamino)-2-methylpropion aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 2,3-dichlorobenzylamine and 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride with 2-trifluoromethylbenzyl amine and 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride, respectively, to give the title compound.

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.38-7.68(m, 7H), 7.17(d, 2H), 6.98(s, 1H), 6.42(bs, 1H), 5.26(s, 2H), 3.91(s, 2H), 3.28(s, 2H), 2.59(s, 2H), 1.27(s, 6H)

<Step 2>

N-(2-Trifluoromethylbenzyl)-N-allylthiocarbamoyl-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

To a solution of N-(2-trifluoromethylbenzyl)-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added allylisothiocyanate (0.1M in CH_2Cl_2 , 0.2ml, 0.02mmol). The reaction mixture was agitated for 3hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: $\text{CH}_2\text{Cl}_2/\text{MeOH}=9/1$, v/v) to give the title compound as a white solid.

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.65(d, 2H), 7.55(m, 3H), 7.17(d, 3H), 7.00(s, 1H), 5.80(m, 1H), 5.35(s, 2H), 5.07(m, 4H), 4.20(t, 2H), 4.00(s, 2H), 3.25(s, 2H), 1.40(s, 6H)

Examples 715-760

N-(2-Trifluoromethylbenzyl)-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 714 to give the title compounds.

Example 715

N-(2-Trifluoromethylbenzyl)-N-benzylthiocarbamoyl-2-{{1-(4-cyanobenzyl)-1

H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.63(m, 5H), 7.45(m, 2H), 7.20(m, 6H), 7.05(bs, 1H), 7.00(s, 1H), 5.30(s, 2H), 5.05(s, 2H), 4.80(d, 2H), 4.20(t, 2H), 4.00(s, 2H), 3.20(s, 2H), 1.40(s, 6H)

Example 716

N-(2-Trifluoromethylbenzyl)-N-(2-biphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(m, 3H), 7.25-7.50(m, 11H), 7.10(d, 3H), 7.00(s, 2H), 5.28(s, 2H), 5.00(s, 2H), 3.90(bs, 2H), 3.20(s, 2H), 1.40(s, 6H)

Example 717

N-(2-Trifluoromethylbenzyl)-N-(2-bromophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.75(d, 1H), 7.45-7.70(m, 6H), 7.37(m, 3H), 7.12(d, 3H), 7.00(s, 1H), 5.30(s, 4H), 4.14(s, 2H), 3.27(s, 2H), 1.45(s, 6H)

Example 718

N-(2-Trifluoromethylbenzyl)-N-(3-bromophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.40-7.65(m, 6H), 7.20-7.37(m, 4H), 7.10(d, 2H), 6.95(s, 1H), 5.40(s, 2H), 5.30(s, 2H), 3.96(s, 2H), 3.28(s, 2H), 1.43(s, 6H)

Example 719

N-(2-Trifluoromethylbenzyl)-N-(4-bromophenylthiocarbamoyl)-2- $\{[1-(4\text{-cyano benzyl})\text{-}1\text{H-imidazol-}5\text{-yl]acetyl}\}$ amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.60(d, 3H), 7.42(d, 4H), 7.27(m, 3H), 7.07(d, 2H), 6.95(s, 1H), 5.40(s, 2H), 5.22(s, 2H), 3.95(s, 2H), 3.25(s, 2H), 1.40(s, 6H)

Example 720

N-(2-Trifluoromethylbenzyl)-N-(n-butylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-}5\text{-yl]acetyl}\}$ amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.60(d, 2H), 7.55(m, 3H), 7.17(d, 3H), 7.00(s, 1H), 5.40(s, 2H), 5.00(s, 2H), 4.00(s, 2H), 3.25(s, 2H), 1.40(s, 6H), 1.30(m, 2H), 1.10(q, 2H), 0.82(t, 3H)

Example 721

N-(2-Trifluoromethylbenzyl)-N-isobutylthiocarbamoyl-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-}5\text{-yl]acetyl}\}$ amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.40-7.68(m, 5H), 7.15(m, 3H), 7.00(s, 1H), 5.38(s, 2H), 5.00(s, 2H), 4.08(s, 2H), 3.38(m, 2H), 3.25(s, 2H), 1.75(m, 1H), 1.42(s, 6H), 0.66(d, 6H)

Example 722

N-(2-Trifluoromethylbenzyl)-N-(*t*-butylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})\text{-}1\text{H-imidazol-}5\text{-yl]acetyl}\}$ amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.90(s, 1H), 7.73(d, 1H), 7.65(d, 2H), 7.55(m, 3H), 7.20(m, 3H), 7.02(s, 1H), 5.40(s, 2H), 4.90(s, 2H), 4.10(s, 2H), 3.27(s,

2H), 1.45(s, 6H), 1.28(s, 9H)

Example 723

N-(2-Trifluoromethylbenzyl)-N-(2-chlorophenylthiocarbamoyl)-2-[[1-(4-cyano benzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.73(d, 1H), 7.60(d, 2H), 7.45(m, 2H), 7.20-7.40(m, 4H), 7.15(d, 2H), 7.00(s, 1H), 5.30(s, 4H), 4.12(s, 2H), 3.25(s, 2H), 1.45(s, 6H)

Example 724

N-(2-Trifluoromethylbenzyl)-N-(3-chlorophenylthiocarbamoyl)-2-[[1-(4-cyano benzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.73(d, 1H), 7.58(d, 3H), 7.25-7.50(m, 6H), 7.17(m, 1H), 7.05(d, 2H), 6.95(s, 1H), 5.40(s, 2H), 5.30(s, 2H), 3.95(s, 2H), 3.25(s, 2H), 1.40(s, 6H)

Example 725

N-(2-Trifluoromethylbenzyl)-N-(4-chlorophenylthiocarbamoyl)-2-[[1-(4-cyano benzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.73(d, 1H), 7.58(d, 3H), 7.45(m, 2H), 7.22(m, 5H), 7.05(d, 2H), 6.95(s, 1H), 5.40(s, 2H), 5.20(s, 2H), 3.98(s, 2H), 3.25(s, 2H), 1.40(s, 6H)

Example 726

N-(2-Trifluoromethylbenzyl)-N-(3-chloro-2-methylphenylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.58(d, 3H), 7.43(m, 2H), 7.28(m, 2H), 7.20(m, 2H), 7.07(d, 2H), 6.95(s, 1H), 5.35(s, 2H), 5.30(s, 2H), 3.98(s, 2H), 3.25(s, 2H), 2.38(s, 3H), 1.42(s, 6H)

Example 727

N-(2-Trifluoromethylbenzyl)-N-cyclohexylthiocarbamoyl-2- $\{[1-(4\text{-cyanobenzyl})-1\text{H-imidazol-5-yl}]acetyl\}$ amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.40-7.65(m, 5H), 7.17(m, 3H), 7.00(s, 1H), 5.40(s, 1H), 5.25(s, 1H), 5.00(s, 1H), 4.10(m, 2H), 3.90(s, 1H), 3.25(s, 2H), 1.90(m, 4H), 1.40(s, 6H), 1.25(s, 6H)

Example 728

N-(2-Trifluoromethylbenzyl)-N-cyclopentylthiocarbamoyl-2- $\{[1-(4\text{-cyanobenzyl})-1\text{H-imidazol-5-yl}]acetyl\}$ amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.20-7.50(m, 5H), 7.17(m, 3H), 7.00(s, 1H), 5.40(s, 2H), 4.95(s, 2H), 4.58(m, 1H), 4.05(s, 2H), 3.25(s, 2H), 2.00(m, 4H), 1.40(s, 6H), 1.25(s, 4H)

Example 729

N-(2-Trifluoromethylbenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2- $\{[1-(4\text{-cyanobenzyl})-1\text{H-imidazol-5-yl}]acetyl\}$ amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.60(d, 4H), 7.45(m, 2H), 7.30(m, 3H), 7.12(d, 3H), 7.00(s, 1H), 5.30(s, 2H), 4.10(s, 2H), 3.25(s, 2H), 1.40(s, 6H)

Example 730

N-(2-Trifluoromethylbenzyl)-N-[2-(dimethylamino)ethylthiocarbamoyl]-2- $\{[1-$

(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.90(bs, 1H), 7.73(d, 1H), 7.62(d, 2H), 7.45(m, 3H), 7.17(d, 3H), 7.05(s, 1H), 5.92(bs, 1H), 5.40(s, 2H), 5.00(s, 2H), 4.05(s, 2H), 3.50(s, 2H), 3.25(s, 2H), 2.38(m, 2H), 1.82(s, 6H), 1.40(s, 6H)

Example 731

N-(2-Trifluoromethylbenzyl)-N-[4-(dimethylamino)phenylthiocarbamoyl]-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.60(m, 4H), 7.45(m, 2H), 7.35(d, 1H), 7.12(d, 2H), 7.00(s, 1H), 6.98(s, 2H), 6.65(d, 2H), 5.35(s, 2H), 5.22(s, 2H), 4.05(s, 2H), 3.25(s, 2H), 2.95(s, 6H), 1.45(s, 6H)

Example 732

N-(2-Trifluoromethylbenzyl)-N-[3-(dimethylamino)propylthiocarbamoyl]-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 9.12(bs, 1H), 7.73(d, 1H), 7.65(d, 2H), 7.45(m, 3H), 7.19(d, 2H), 7.03(m, 2H), 5.40(s, 2H), 4.96(s, 2H), 3.90(s, 2H), 3.70(m, 2H), 3.25(s, 2H), 2.40(m, 2H), 1.90(s, 6H), 1.72(m, 2H), 1.40(s, 6H)

Example 733

N-(2-Trifluoromethylbenzyl)-N-ethoxycarbonylthiocarbamoyl-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.50-7.70(m, 6H), 7.40(m, 1H), 7.17(d, 2H), 7.00(m, 1H), 5.35(m, 4H), 5.00(bs, 2H), 4.20(q, 4H), 3.30(s, 2H), 1.40(s,

6H), 1.25(d, 3H)

Example 734

N-(2-Trifluoromethylbenzyl)-N-ethoxycarbonylmethylthiocarbamoyl-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl} amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.73(d, 1H), 7.62(d, 2H), 7.40-7.58(m, 3H), 7.18(d, 3H), 7.00(s, 1H), 5.38(s, 2H), 5.12(s, 2H), 4.33(d, 2H), 4.19(q, 2H), 4.00(s, 2H), 3.25(s, 2H), 1.40(s, 6H), 1.25(t, 3H)

Example 735

N-(2-Trifluoromethylbenzyl)-N-(3-ethoxypropylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl} amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 8.90(bs, 1H), 7.73(d, 1H), 7.65(d, 2H), 7.55(m, 3H), 7.20(d, 2H), 7.05(m, 2H), 5.82(s, 1H), 5.40(s, 2H), 5.00(s, 2H), 3.97(s, 2H), 3.72(q, 2H), 3.40(t, 2H), 3.25(s, 2H), 3.20(t, 2H), 1.80(q, 2H), 1.40(s, 6H), 0.90(t, 3H)

Example 736

N-(2-Trifluoromethylbenzyl)-N-ethylthiocarbamoyl-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl} amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.73(d, 1H), 7.65(d, 2H), 7.45(m, 3H), 7.17(d, 3H), 7.00(s, 1H), 5.40(s, 2H), 5.05(s, 2H), 4.00(s, 2H), 3.60(m, 2H), 3.25(s, 2H), 1.40(s, 6H), 1.07(t, 3H)

Example 737

N-(2-Trifluoromethylbenzyl)-N-(2-fluorophenylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl} amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.73(d, 1H), 7.60(m, 3H), 7.45(m, 3H), 7.20(m, 1H), 7.12(d, 4H), 6.95(s, 1H), 5.30(s, 4H), 3.96(s, 2H), 3.25(s, 2H), 1.44(s, 6H)

Example 738

N-(2-Trifluoromethylbenzyl)-N-(3-fluorophenylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.73(d, 1H), 7.58(d, 3H), 7.45(m, 2H), 7.10-7.32(m, 4H), 7.07(d, 2H), 6.92(m, 2H), 5.40(bs, 2H), 5.25(s, 2H), 3.97(s, 2H), 3.26(s, 2H), 1.42(s, 6H)

Example 739

N-(2-Trifluoromethylbenzyl)-N-(4-fluorophenylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.73(d, 1H), 7.60(d, 3H), 7.45(m, 3H), 7.25(m, 4H), 7.10(d, 2H), 7.00(d, 2H), 5.30(s, 2H), 5.25(s, 2H), 4.00(s, 2H), 3.25(s, 2H), 1.41(s, 6H)

Example 740

N-(2-Trifluoromethylbenzyl)-N-(4-hydroxyphenylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

(CDCl₃, CD₃-OD) 7.73(d, 1H), 7.60(d, 3H), 7.43(m, 2H), 7.30(d, 1H), 7.10(m, 4H), 6.95(s, 1H), 6.80(d, 2H), 5.35(s, 2H), 5.30(s, 2H), 4.00(s, 2H), 3.25(s, 2H), 1.41(s, 6H)

Example 741

N-(2-Trifluoromethylbenzyl)-N-(4-isopropylphenylthiocarbamoyl)-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.58(m, 3H), 7.45(m, 2H), 7.30(m, 2H), 7.20(s, 3H), 7.10(d, 2H), 7.00(s, 1H), 5.30(s, 4H), 4.00(s, 2H), 3.25(s, 2H), 2.90(q, 1H), 1.43(s, 6H), 1.12(d, 6H)

Example 742

N-(2-Trifluoromethylbenzyl)-N-(2-methoxyethylthiocarbamoyl)-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.60(bs, 1H), 7.73(d, 1H), 7.60(d, 2H), 7.50(m, 3H), 7.17(d, 3H), 7.00(s, 1H), 6.20(bs, 1H), 5.40(s, 2H), 5.00(s, 2H), 4.03(s, 2H), 3.70(q, 2H), 3.37(t, 2H), 3.25(s, 2H), 3.06(s, 3H), 1.42(s, 6H)

Example 743

N-(2-Trifluoromethylbenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.70(s, 1H), 8.12(d, 1H), 7.76(d, 1H), 7.63(m, 1H), 7.57(d, 2H), 7.50(m, 2H), 7.30(d, 1H), 7.17(d, 3H), 7.00(m, 2H), 6.80(d, 1H), 5.38(s, 2H), 5.20(s, 2H), 4.20(s, 2H), 3.52(s, 3H), 3.25(s, 2H), 1.45(s, 6H)

Example 744

N-(2-Trifluoromethylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2-{{1-(4-cyanobenzyl)-1H-imidazol-5-yl}acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.60(m, 3H), 7.45(m, 2H), 7.30(d,

1H), 7.12(d, 4H), 7.00(s, 1H), 6.85(d, 2H), 5.30(s, 4H), 4.00(s, 2H), 3.80(s, 3H), 3.25(s, 2H), 1.45(s, 6H)

Example 745

N-(2-Trifluoromethylbenzyl)-N-(3-methoxypropylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 9.00(bs, 1H), 7.73(d, 1H), 7.65(d, 2H), 7.45(m, 3H), 7.17(d, 2H), 7.05(m, 3H), 5.40(s, 2H), 4.95(s, 2H), 4.00(s, 2H), 3.70(q, 2H), 3.35(t, 2H), 3.25(s, 2H), 2.85(s, 3H), 1.78(p, 2H), 1.40(s, 6H)

Example 746

N-(2-Trifluoromethylbenzyl)-N-(2-methoxypyridin-5-ylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.90(bs, 1H), 7.73(d, 1H), 7.60(d, 4H), 7.45(m, 2H), 7.30(d, 1H), 7.10(d, 2H), 6.95(s, 1H), 6.75(d, 1H), 5.80(m, 1H), 5.38(s, 2H), 5.25(s, 2H), 4.00(s, 2H), 3.93(s, 3H), 3.25(s, 2H), 1.42(s, 6H)

Example 747

N-(2-Trifluoromethylbenzyl)-N-methylthiocarbamoyl-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.73(d, 1H), 7.65(d, 2H), 7.45(m, 4H), 7.17(d, 2H), 7.12(s, 1H), 7.00(s, 1H), 5.38(s, 2H), 5.10(s, 2H), 3.95(s, 2H), 3.25(s, 2H), 3.08(d, 3H), 1.40(s, 6H)

Example 748

N-(2-Trifluoromethylbenzyl)-N-(4-methylthiophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.58(d, 3H), 7.45(m, 3H), 7.30(d, 1H), 7.20(s, 3H), 7.10(d, 2H), 6.95(s, 1H), 5.80(m, 1H), 5.35(s, 2H), 5.25(s, 2H), 4.00(s, 2H), 3.25(s, 2H), 2.48(s, 3H), 1.42(s, 6H)

Example 749

N-(2-Trifluoromethylbenzyl)-N-(2-naphthylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60-7.82(m, 6H), 7.45(m, 7H), 7.12(d, 1H), 7.00(s, 3H), 5.40(s, 2H), 5.20(s, 2H), 4.00(s, 2H), 3.25(s, 2H), 1.45(s, 6H)

Example 750

N-(2-Trifluoromethylbenzyl)-N-(4-nitrophenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.18(d, 2H), 7.72(d, 2H), 7.55(m, 4H), 7.45(q, 2H), 7.30(s, 1H), 7.10(d, 2H), 6.95(s, 1H), 5.42(s, 2H), 5.25(s, 2H), 3.90(s, 2H), 3.33(s, 2H), 1.43(s, 6H)

Example 751

N-(2-Trifluoromethylbenzyl)-N-(n-pentylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.70(bs, 1H), 7.73(d, 1H), 7.65(d, 2H), 7.50(m, 3H), 7.19(d, 3H), 7.00(s, 1H), 5.40(s, 2H), 5.00(s, 2H), 4.10(s, 2H), 3.43(m, 2H), 3.25(s, 2H), 1.43(s, 6H), 1.25(m, 2H), 0.95(m, 3H), 0.79(t,

2H), 0.61(d, 2H)

Example 752

N-(2-Trifluoromethylbenzyl)-N-phenethylthiocarbamoyl-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.69(s,1H), 7.6d(d, 2H), 7.45(m, 3H), 7.17(d, 5H), 7.00(s, 2H), 6.68(s, 2H), 5.35(s, 2H), 4.90(s, 2H), 4.00(s, 2H), 3.85(q, 2H), 3.25(s, 2H), 2.80(t, 2H), 1.40(s, 6H)

Example 753

N-(2-Trifluoromethylbenzyl)-N-phenylthiocarbamoyl-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.73(d, 1H), 7.58(m, 3H), 7.45(m, 2H), 7.25(m, 6H), 7.07(d, 2H), 7.00(s, 1H), 5.35(s, 2H), 5.25(s, 2H), 4.00(s, 2H), 3.25(s, 2H), 1.42(s, 6H)

Example 754

N-(2-Trifluoromethylbenzyl)-N-(n-propylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.73(d, 1H), 7.65(d, 2H), 7.50(m, 3H), 7.17(d, 3H), 7.00(s, 1H), 5.37(s, 2H), 5.00(s, 2H), 4.00(s, 2H), 3.50(q, 2H), 3.25(s, 2H), 1.40(s, 6H) 1.25(m, 2H), 0.70(t, 3H)

Example 755

N-(2-Trifluoromethylbenzyl)-N-(3-methylphenylthiocarbamoyl)-2- {[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.65(m, 1H), 7.58(d, 2H), 7.45(m, 2H), 7.32(d, 1H), 7.20(d, 1H), 7.10(m, 5H), 7.00(s, 1H), 5.30(s, 2H), 4.00(s, 2H), 3.25(s, 2H), 2.37(s, 3H), 1.40(s, 6H)

Example 756

N-(2-Trifluoromethylbenzyl)-N-(2-methylphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.65(m, 1H), 7.55(d, 2H), 7.40(m, 3H), 7.20(s, 3H), 7.12(d, 3H), 6.95(s, 1H), 5.30(s, 2H), 5.20(s, 2H), 4.10(s, 2H), 3.25(s, 2H), 2.00(s, 3H), 1.40(s, 6H)

Example 757

N-(2-Trifluoromethylbenzyl)-N-(4-methylphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.65(m, 1H), 7.57(d, 2H), 7.45(m, 2H), 7.36(d, 1H), 7.17(s, 6H), 7.00(s, 1H), 5.30(s, 4H), 4.00(s, 2H), 3.25(s, 2H), 2.36(s, 3H), 1.42(s, 6H)

Example 758

N-(2-Trifluoromethylbenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.73(d, 1H), 7.62(d, 1H), 7.55(d, 3H), 7.45(m, 4H), 7.36(d, 1H), 7.07(d, 3H), 6.94(s, 1H), 5.42(s, 2H), 5.25(s, 2H), 3.95(s, 2H), 3.28(s, 2H), 1.40(s, 6H)

Example 759

N-(2-Trifluoromethylbenzyl)-N-(2,4-dimethylphenylthiocarbamoyl)-2-{[1-(4-c

yanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.75(d, 2H), 7.65(d, 1H), 7.60(d, 2H), 7.50(s, 2H), 7.39(d, 1H), 7.17(d, 2H), 7.00(m, 3H), 5.38(s, 2H), 5.20(s, 2H), 4.00(s, 2H), 3.25(s, 2H), 2.33(s, 3H), 2.00(s, 3H), 1.40(s, 6H)

Example 760

N-(2-Trifluoromethylbenzyl)-N-(3,4-dimethylphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-2-methylpropylamine

¹H-NMR(CDCl₃) : δ 7.75(d, 1H), 7.65(d, 1H), 7.58(d, 2H), 7.45(s, 2H), 7.35(d, 1H), 7.12(d, 3H), 7.00(s, 3H), 5.30(s, 4H), 4.00(s, 2H), 3.25(s, 2H), 2.26(s, 6H), 1.40(s, 6H)

Example 761

N-(2-Trifluoromethylbenzyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino butylamine

<Step 1>

N-(2-Trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

Using the same methods as described in Preparative Example 3, 2(S)-(N-*t*-butoxycarbonyl)aminobutyric acid was converted to 2(S)-(N-*t*-butoxycarbonyl)aminobutyraldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 2,3-dichlorobenzylamine and 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride with 2-trifluoromethylbenzylamine and 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride, respectively, to give the title compound.

¹H-NMR(CDCl₃) : δ 7.64(d, 1H), 7.59(d, 2H), 7.51(s, 3H), 7.13(d, 2H), 7.00(s, 1H), 6.23(d, 1H), 5.28(s, 2H), 3.83-3.93(m, 3H), 3.36(s, 2H), 2.66(d, 2H), 1.35-1.49(m, 2H), 0.85(t, 3H)

<Step 2>

N-(2-Trifluoromethylbenzyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino butylamine

To a solution of N-(2-trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine in dichloromethane (0.02M, 1ml, 0.02 mmol) was added allylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 3hr at room temperature. The mixture was purified by silica gel column chromatography (eluent: CH₂Cl₂/MeOH=9/1, v/v) to give the title compound as a white solid.

¹H-NMR(CDCl₃) : δ 7.65(m, 3H), 7.47(m, 3H), 7.18(m, 3H), 7.00(s, 2H), 6.41(bs, 1H), 5.85(m, 1H), 5.35(q, 3H), 5.05(m, 2H), 4.70(d, 2H), 4.30(t, 2H), 4.00(q, 1H), 3.35(s, 2H), 3.03(dd, 1H), 1.65(m, 1H), 1.45(m, 1H), 0.90(t, 3H)

Examples 762-806

N-(2-Trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 761 to give the title compounds.

Example 762

N-(2-Trifluoromethylbenzyl)-N-benzylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.70(s, 1H), 7.60(d, 2H), 7.45(m, 3H), 7.23(m, 4H), 7.15(m, 4H), 7.00(m, 2H), 6.70(bs, 1H), 5.25(m, 3H), 4.85(d, 2H), 4.70(d, 2H), 4.00(q, 1H), 3.25(s, 2H), 3.05(dd, 1H), 1.58(m, 2H), 0.88(t, 3H)

Example 763

N-(2-Trifluoromethylbenzyl)-N-(2-biphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.60(m, 4H), 7.45(s, 1H), 7.30(m, 10H), 7.12(d, 2H), 6.98(m, 2H), 5.45(bs, 1H), 5.20(s, 2H), 4.62(bs, 1H), 3.80(s, 1H), 3.30(s, 2H), 2.90(dd, 1H), 1.60(m, 1H), 0.85(t, 3H)

Example 764

N-(2-Trifluoromethylbenzyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.72(t, 3H), 7.55(m, 4H), 7.40(m, 3H), 7.32(m, 1H), 7.12(m, 3H), 7.00(s, 2H), 5.45(bs, 1H), 5.25(s, 2H), 4.85(d, 2H), 4.20(m, 1H), 3.40(s, 2H), 3.15(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 765

N-(2-Trifluoromethylbenzyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 9.10(s, 1H), 7.70(d, 1H), 7.55(m, 4H), 7.45(s, 2H),

7.20-7.40(m, 4H), 7.10(d, 2H), 6.95(s, 1H), 6.85(d, 1H), 5.90(d, 1H), 5.29(s, 2H), 4.74(d, 1H), 4.40(s, 1H), 4.00(s, 1H), 3.40(s, 2H), 3.02(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 766

N-(2-Trifluoromethylbenzyl)-N-(4-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 8.80(s, 1H), 7.70(d, 1H), 7.56(d, 2H), 7.45(d, 4H), 7.35(m, 3H), 7.08(d, 2H), 6.95(s, 1H), 6.80(d, 1H), 5.80(d, 1H), 5.22(s, 2H), 4.76(d, 1H), 4.41(s, 1H), 4.00(m, 1H), 3.39(s, 2H), 3.04(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 767

N-(2-Trifluoromethylbenzyl)-N-n-butylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.66(m, 3H), 7.45(m, 3H), 7.20(m, 3H), 7.10(m, 3H), 7.00(s, 1H), 6.20(bs, 1H), 5.35(m, 3H), 4.70(d, 2H), 4.00(m, 1H), 3.60(m, 2H), 3.34(s, 2H), 3.02(dd, 1H), 1.60(m, 1H), 1.50(m, 3H), 1.18(m, 2H), 0.88(m, 6H)

Example 768

N-(2-Trifluoromethylbenzyl)-N-isobutylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.65(m, 3H), 7.52(m, 2H), 7.40(m, 2H), 7.18(m, 3H), 7.00(s, 1H), 6.00(s, 1H), 5.34(q, 2H), 5.12(m, 1H), 4.85(m, 1H), 4.70(d, 1H), 4.02(s, 1H), 3.50(m, 1H), 3.34(s, 3H), 3.05(dd, 1H), 1.80(m, 1H), 1.50(m, 2H), 0.90(t, 3H), 0.75(m, 6H)

Example 769

N-(2-Trifluoromethylbenzyl)-N-(*t*-butylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.71(m, 1H), 7.65(d, 2H), 7.55(m, 2H), 7.45(m, 2H), 7.18(d, 2H), 7.05(s, 1H), 5.36(q, 2H), 5.15(m, 1H), 4.75(q, 2H), 4.00(m, 1H), 3.35(s, 2H), 3.05(dd, 1H), 1.55(m, 2H), 1.31(s, 9H), 0.90((t, 3H)

Example 770

N-(2-Trifluoromethylbenzyl)-N-(2-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.90(bs, 1H), 7.72(t, 2H), 7.60(m, 3H), 7.42(m, 4H), 7.25(m, 2H), 7.10(d, 2H), 7.00(s, 1H), 6.95(bs, 1H), 5.46(bs, 1H), 5.25(s, 2H), 4.85(d, 1H), 4.80(s, 1H), 4.20(m, 1H), 3.40(s, 2H), 3.12(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90((t, 3H)

Example 771

N-(2-Trifluoromethylbenzyl)-N-(3-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 9.05(bs, 1H), 7.70(d, 1H), 7.60(d, 3H), 7.42(m, 5H), 7.20(m, 2H), 7.10(d, 2H), 6.95(s, 1H), 6.85(ds, 1H), 5.90(d, 1H), 5.28(s, 2H), 4.80(d, 1H), 4.40(s, 1H), 4.00(m, 1H), 3.40(s, 2H), 3.05(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90((t, 3H)

Example 772

N-(2-Trifluoromethylbenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cy

anobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.80(bs, 1H), 7.70(d, 1H), 7.60(d, 3H), 7.40(s, 2H), 7.30(m, 5H), 7.10(d, 2H), 6.95(s, 1H), 6.80(s, 1H), 5.80(d, 1H), 5.23(s, 2H), 4.80(d, 1H), 4.42(s, 1H), 4.00(m, 1H), 3.38(s, 2H), 3.05(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 773

N-(2-Trifluoromethylbenzyl)-N-(3-chloro-4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.85(bs, 1H), 7.70(d, 1H), 7.56(d, 3H), 7.45(s, 1H), 7.38(m, 3H), 7.25(m, 2H), 7.10(d, 2H), 6.95(s, 1H), 6.88(d, 1H), 5.80(d, 1H), 5.27(s, 2H), 4.80(d, 1H), 4.42(s, 1H), 4.00(m, 1H), 3.38(s, 2H), 3.05(dd, 1H), 2.30(s, 3H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 774

N-(2-Trifluoromethylbenzyl)-N-cyclohexylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(m, 3H), 7.52(s, 1H), 7.43(m, 2H), 7.18(m, 3H), 7.00(s, 2H), 5.80(bs, 1H), 5.35(s, 3H), 5.11(m, 1H), 4.82(m, 1H), 4.75(d, 1H), 4.22(m, 1H), 4.00(m, 1H), 3.38(s, 2H), 3.02(dd, 1H), 1.90(m, 2H), 1.20-1.65(m, 8H), 1.10(m, 2H), 0.90(t, 3H)

Example 775

N-(2-Trifluoromethylbenzyl)-N-cyclopentylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(m, 3H), 7.52(s, 1H), 7.43(m, 2H), 7.18(m,

3H), 7.00(s, 1H), 5.95(m, 1H), 5.35(q, 2H), 5.20(m, 1H), 4.80(m, 1H), 4.64(m, 2H), 4.01(m, 1H), 3.35(s, 2H), 3.05(dd, 1H), 2.00(m, 2H), 1.20-1.70(m, 8H), 0.87(t, 3H)

Example 776

N-(2-Trifluoromethylbenzyl)-N-(2,4-dichlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.20(bs, 1H), 7.75(d, 2H), 7.60(m, 3H), 7.40(m, 4H), 7.28(m, 1H), 7.15(m, 2H), 7.00(s, 1H), 6.81(s, 1H), 5.55(bs, 1H), 5.25(s, 2H), 4.83(d, 1H), 4.70(bs, 1H), 4.18(m, 1H), 3.40(s, 2H), 3.16(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.95(t, 3H)

Example 777

N-(2-Trifluoromethylbenzyl)-N-[2-(dimethylamino)ethylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(m, 3H), 7.42(m, 4H), 7.18(m, 3H), 7.05(s, 1H), 6.78(bs, 1H), 4.65-5.05(m, 2H), 4.10(m, 1H), 3.50(s, 2H), 3.38(s, 2H), 3.14(dd, 1H), 2.40(m, 2H), 1.90(s, 6H), 1.50(m, 2H), 0.90(t, 3H)

Example 778

N-(2-Trifluoromethylbenzyl)-N-[4-(dimethylamino)phenylthiocarbamoyl]-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.90(bs, 1H), 7.70(d, 1H), 7.58(d, 3H), 7.48(m, 2H), 7.40(t, 2H), 7.10(t, 3H), 7.00(s, 1H), 6.65(d, 2H), 5.45(d, 1H), 5.28(s, 2H), 4.80(d, 2H), 4.08(m, 1H), 3.38(s, 2H), 3.10(dd, 1H), 2.95(s, 6H), 1.60(m, 2H), 0.90(t, 3H)

Example 779

N-(2-Trifluoromethylbenzyl)-N-[3-(dimethylamino)propylthiocarbamoyl]-2(S)-
-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 9.90(bs, 1H), 7.72(s, 1H), 7.65(d, 2H), 7.42(m, 3H), 7.20(d, 2H), 7.05(d, 1H), 7.00(s, 1H), 5.40(q, 2H), 5.00(m, 1H), 4.70(s, 2H), 4.01(m, 1H), 3.70(m, 2H), 3.32(q, 2H), 2.90(dd, 1H), 2.38(m, 2H), 1.79(s, 8H), 1.50(p, 2H), 0.87(t, 3H)

Example 780

N-(2-Trifluoromethylbenzyl)-N-ethoxycarbonylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.65(m, 3H), 7.50(m, 2H), 7.42(d, 1H), 7.30(s, 1H), 7.18(d, 2H), 7.02(d, 1H), 6.25(m, 1H), 5.32(m, 3H), 4.90(d, 1H), 4.65(d, 1H), 4.18(q, 2H), 4.05(bs, 1H), 3.38(s, 2H), 3.00(m, 1H), 1.70(m, 2H), 1.25(m, 2H), 0.88(m, 4H)

Example 781

N-(2-Trifluoromethylbenzyl)-N-(3-ethoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.65(m, 3H), 7.42(m, 4H), 7.18(m, 3H), 7.00(s, 1H), 6.82(bs, 1H), 5.38(q, 2H), 4.90(m, 2H), 4.68(d, 1H), 4.00(m, 1H), 3.75(q, 2H), 3.42(m, 2H), 3.38(s, 2H), 3.18(m, 2H), 2.98(dd, 1H), 1.80(p, 2H), 1.50(m, 2H), 0.85(q, 6H)

Example 782

N-(2-Trifluoromethylbenzyl)-N-ethylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(m, 3H), 7.45(m, 3H), 7.18(m, 3H), 7.00(s, 2H), 6.30(bs, 1H), 5.33(q 3H), 4.65(d, 2H), 4.00(m, 1H), 3.65(m, 2H), 3.38(s, 2H), 3.00(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 1.12(t, 3H), 0.90(t, 3H)

Example 783

N-(2-Trifluoromethylbenzyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.20(bs, 1H), 7.71(d, 2H), 7.58(m, 3H), 7.43(m, 3H), 7.18(m, 5H), 7.00(m, 2H), 5.60(d, 1H), 5.26(q 3H), 4.85(d, 1H), 4.52(s, 1H), 4.10(m, 1H), 3.39(s, 2H), 3.10(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 784

N-(2-Trifluoromethylbenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.95(s, 1H), 7.70(d, 1H), 7.57(m, 3H), 7.45(s, 1H), 7.40(m, 2H), 7.25(m, 3H), 7.10(d, 2H), 6.97(s, 1H), 6.85(m, 2H), 5.85(d, 1H), 5.28(s, 3H), 4.75(d, 2H), 4.45(m, 1H), 4.00(m, 1H), 3.38(s, 2H), 3.08(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 785

N-(2-Trifluoromethylbenzyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.60(s, 1H), 7.72(d, 1H), 7.58(m, 4H), 7.35(m, 4H), 7.10(t, 3H), 7.00(s, 2H), 6.83(d, 1H), 5.73(d, 1H), 5.28(s, 2H),

4.80(d, 1H), 4.50(bs, 1H), 4.00(m, 1H), 3.38(s, 2H), 3.08(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 786

N-(2-Trifluoromethylbenzyl)-N-(4-hydroxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CD}_3\text{OD})$: δ 7.75(m, 2H), 7.62(m, 3H), 7.40(m, 2H), 7.23(d, 2H), 7.10(d, 2H), 6.95(s, 1H), 6.75(d, 2H), 5.60(d, 1H), 5.38(s, 2H), 5.10(d, 1H), 4.03(m, 2H), 3.43(q, 2H), 3.30(m, 1H), 3.08(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 787

N-(2-Trifluoromethylbenzyl)-N-(4-isopropylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.20(bs, 1H), 7.70(d, 1H), 7.57(d, 3H), 7.50(m, 1H), 7.40(t, 2H), 7.23(m, 4H), 7.20(d, 2H), 7.00(s, 2H), 5.60(d, 1H), 5.26(s, 2H), 4.80(d, 1H), 4.70(bs, 1H), 4.05(m, 1H), 3.38(s, 2H), 3.08(dd, 1H), 2.90(m, 1H), 1.70(m, 1H), 1.50(m, 1H), 1.12(d, 6H), 0.90(t, 3H)

Example 788

N-(2-Trifluoromethylbenzyl)-N-(2-methoxyethylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(m, 3H), 7.52(s, 1H), 7.42(t, 2H), 7.20(d, 4H), 7.00(s, 1H), 6.20(s, 1H), 5.35(q, 2H), 4.98(m, 2H), 4.70(d, 1H), 4.08(m, 1H), 3.75(m, 2H), 3.40(m, 2H), 3.33(s, 2H), 3.10(s, 4H), 1.65(m, 2H), 0.90(t, 3H)

Example 789

N-(2-Trifluoromethylbenzyl)-N-(2-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 8.22(d, 1H), 7.77(d, 1H), 7.65(s, 1H), 7.50(m, 5H), 7.25(m, 2H), 7.07(m, 5H), 6.90(d, 1H), 5.28(s, 2H), 5.10(s, 2H), 4.90(d, 1H), 4.20(m, 1H), 3.58(s, 3H), 3.38(s, 2H), 3.18(dd, 1H), 1.60(m, 2H), 0.90(t, 3H)

Example 790

N-(2-Trifluoromethylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 8.22(bs, 1H), 7.70(d, 1H), 7.58(d, 2H), 7.45(m, 2H), 7.40(t, 2H), 7.20(d, 2H), 7.10(d, 2H), 7.00(s, 2H), 6.85(d, 2H), 5.60(d, 1H), 5.28(s, 2H), 4.80(d, 1H), 4.65(m, 1H), 4.02(m, 1H), 3.80(s, 3H), 3.38(s, 2H), 3.08(dd, 1H), 1.60(m, 2H), 0.90(t, 3H)

Example 791

N-(2-Trifluoromethylbenzyl)-N-(3-methoxypropylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.72(d, 1H), 7.65(d, 2H), 7.45(m, 4H), 7.20(d, 2H), 7.10(d, 1H), 7.00(s, 1H), 6.90(s, 1H), 5.38(q, 2H), 4.90(m, 2H), 4.70(d, 1H), 4.02(m, 1H), 3.72(m, 2H), 3.40(m, 2H), 3.58(s, 3H), 3.33(s, 2H), 3.00(dd, 1H), 2.85(s, 3H), 1.80(m, 2H), 1.50(m, 2H), 0.90(t, 3H)

Example 792

N-(2-Trifluoromethylbenzyl)-N-(2-methoxypyridin-5-ylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.80(bs, 1H), 8.00(d, 1H), 7.77(d, 2H), 7.58(d, 3H), 7.40(m, 3H), 7.10(d, 2H), 6.90(m, 2H), 6.75(d, 1H), 5.80(d, 1H), 5.28(s, 2H), 4.70(d, 1H), 4.50(s, 1H), 4.02(m, 1H), 3.90(s, 3H), 3.38(s, 2H), 3.06(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 793

N-(2-Trifluoromethylbenzyl)-N-methylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(m, 3H), 7.45(m, 3H), 7.20(m, 3H), 7.00(m, 2H), 6.70(s, 1H), 5.32(m, 3H), 4.65(d, 1H), 4.55(s, 1H), 4.00(m, 1H), 3.38(s, 2H), 3.12(d, 3H), 2.96(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 794

N-(2-Trifluoromethylbenzyl)-N-(4-methylthiophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.50(bs, 1H), 7.70(d, 1H), 7.58(d, 3H), 7.32-7.46(m, 4H), 7.25(d, 3H), 7.10(d, 2H), 7.00(s, 1H), 6.90(s, 1H), 5.70(d, 1H), 5.25(s, 2H), 4.80(d, 1H), 4.55(s, 1H), 4.01(m, 1H), 3.38(s, 2H), 3.06(dd, 1H), 2.45(s, 3H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 795

N-(2-Trifluoromethylbenzyl)-N-(2-naphthylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.80(bs, 1H), 7.68-7.83(m, 5H), 7.58(d, 2H), 7.22(m, 7H), 7.00(m, 3H), 6.88(d, 1H), 5.80(d, 1H), 5.20(s, 2H), 4.82(d,

1H), 4.60(s, 1H), 4.05(m, 1H), 3.38(s, 2H), 3.09(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 796

N-(2-Trifluoromethylbenzyl)-N-(4-nitrophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 9.60(bs, 1H), 8.20(d, 2H), 7.80(d, 2H), 7.70(d, 1H), 7.55(m, 4H), 7.40(m, 2H), 7.10(d, 2H), 7.00(d, 2H), 6.75(d, 1H), 6.02(d, 1H), 5.23(s, 2H), 4.80(d, 1H), 4.25(m, 1H), 3.98(s, 1H), 3.40(s, 2H), 3.09(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 797

N-(2-Trifluoromethylbenzyl)-N-(n-pentylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.70(m, 3H), 7.48(m, 3H), 7.20(m, 4H), 7.00(s, 1H), 5.90(s, 1H), 5.38(q, 2H), 5.00(m, 2H), 4.70(d, 1H), 4.02(m, 1H), 3.60(m, 1H), 3.45(m, 1H), 3.35(s, 2H), 3.06(dd, 1H), 1.68(m, 4H), 1.10(m, 2H), 0.90(t, 3H), 0.75(m, 5H)

Example 798

N-(2-Trifluoromethylbenzyl)-N-phenethylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.62(m, 3H), 7.50(s, 1H), 7.40(m, 2H), 7.15(m, 5H), 7.00(m, 4H), 6.10(bs, 1H), 5.32(q, 2H), 5.05(m, 1H), 4.70(m, 1H), 4.60(d, 1H), 3.90(m, 3H), 3.36(s, 2H), 3.00(dd, 1H), 2.85(t, 2H), 1.57(m, 2H), 0.90(t, 3H)

Example 799

N-(2-Trifluoromethylbenzyl)-N-phenylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.50(bs, 1H), 7.72(d, 1H), 7.58(d, 3H), 7.40(s, 2H), 7.18-7.40(m, 6H), 7.10(d, 2H), 7.00(s, 1H), 6.95(s, 1H), 5.70(d, 1H), 5.28(s, 2H), 4.80(d, 1H), 4.62(s, 1H), 4.02(m, 1H), 3.38(s, 2H), 3.09(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 800

N-(2-Trifluoromethylbenzyl)-N-(n-propylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.65(m, 3H), 7.46(m, 3H), 7.20(m, 3H), 7.05(m, 2H), 6.20(s, 1H), 5.30(s, 3H), 4.70(d, 2H), 4.00(m, 1H), 3.58(m, 2H), 3.38(s, 2H), 3.03(dd, 1H), 1.50(m, 4H), 0.90(t, 3H), 0.80(t, 3H)

Example 801

N-(2-Trifluoromethylbenzyl)-N-(3-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.30(bs, 1H), 7.72(d, 1H), 7.55(d, 3H), 7.50(s, 1H), 7.40(t, 2H), 7.02-7.24(m, 5H), 7.00(m, 2H), 5.60(d, 1H), 5.25(s, 2H), 4.80(d, 1H), 4.65(m, 1H), 4.02(m, 1H), 3.38(s, 2H), 3.06(dd, 1H), 2.32(s, 3H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 802

N-(2-Trifluoromethylbenzyl)-N-(2-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.72(d, 1H), 7.55(m, 3H), 7.42(m, 4H), 7.18(m, 7H), 7.00(s, 1H), 5.50(d, 1H), 5.26(s, 2H), 4.88(d, 2H), 4.12(m, 1H), 3.38(s, 2H), 3.12(dd, 1H), 2.10(s, 3H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 803

N-(2-Trifluoromethylbenzyl)-N-(4-methylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.30(bs, 1H), 7.72(d, 1H), 7.55(d, 3H), 7.40(m, 3H), 7.18(m, 5H), 7.00(m, 2H), 5.60(d, 1H), 5.25(s, 2H), 4.80(d, 1H), 4.65(m, 1H), 4.02(m, 1H), 3.38(s, 2H), 3.06(dd, 1H), 2.32(s, 3H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 804

N-(2-Trifluoromethylbenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 9.40(bs, 1H), 7.90(s, 1H), 7.70(m, 2H), 7.55(d, 3H), 7.40(m, 5H), 7.05(d, 2H), 6.95(s, 1H), 6.85(d, 1H), 6.00(d, 1H), 5.25(s, 2H), 4.80(d, 1H), 4.30(m, 1H), 4.00(m, 1H), 3.38(s, 2H), 3.03(dd, 1H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 805

N-(2-Trifluoromethylbenzyl)-N-(2,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.72(d, 1H), 7.60(d, 3H), 7.41(m, 4H), 7.10(d, 3H), 7.00(s, 4H), 5.45(m, 1H), 5.26(s, 2H), 4.80(d, 2H), 4.12(m, 1H), 3.38(s, 2H), 3.12(dd, 1H), 2.35(s, 3H), 2.05(s, 3H), 1.70(m, 1H), 1.50(m,

1H), 0.90(t, 3H)

Example 806

N-(2-Trifluoromethylbenzyl)-N-(3,4-dimethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminobutylamine

¹H-NMR(CDCl₃) : δ 7.72(d, 1H), 7.60(d, 3H), 7.41(m, 4H), 7.10(d, 3H), 7.00(s, 4H), 5.45(m, 1H), 5.26(s, 2H), 4.80(d, 2H), 4.12(m, 1H), 3.38(s, 2H), 3.12(dd, 1H), 2.35(s, 3H), 2.05(s, 3H), 1.70(m, 1H), 1.50(m, 1H), 0.90(t, 3H)

Example 807

N-(2-Chlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

<Step 1>

N-(2-Chlorobenzyl)-2(S)-(*t*-butoxycarbonyl)amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Preparative Example 4 <Step1>, but replacing 2,3-dichlorobenzylamine with 2-chlorobenzylamine.

¹H-NMR (CDCl₃) : δ 7.4(m, 2H), 7.2(m, 2H), 4.6 (bs, 1H), 3.9(m, 2H), 3.6 (bs, 1H), 2.6 (t, 2H), 1.4(s, 9H), 1.1-1.6(m, 3H), 0.8(m, 6H)

<Step 2>

N-(2-Chlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-(*t*-butoxycarbonyl)amino-3(S)-methylpentylamine

To a solution of N-(2-chlorobenzyl)-2(S)-(*t*-butoxycarbonyl)amino-

3(S)-methylpentylamine (0.50 g, 1.48 mmol) in dichloromethane (10 ml) was added 4-methoxyphenylisothiocyanate (0.20 ml, 1.48 mmol). The reaction mixture was stirred at room temperature for 3hr and concentrated *in vacuo*. The residue was purified by silica gel column chromatography(eluent: n-hexane/CH₂Cl₂=2/1, v/v) to give the title compound.

¹H-NMR (CDCl₃) : δ 7.2-7.4(m, 6H), 6.9(d, 2H), 5.5(m, 1H), 5.1(m, 1H), 4.7(m, 2H), 3.9(m, 1H), 3.8(s, 3H), 3.3(m, 2H), 1.4(s, 9H), 1.2-1.6(m, 3H), 0.9(m, 6H)

<Step 3>

N-(2-Chlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-amino-3(S)-methylpentylamine

A solution of N-(2-chlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-(*t*-butoxycarbonyl)amino-3(S)-methylpentylamine (0.30 g) and trifluoro acetic acid (2 ml) in dichloromethane (10 ml) was stirred at room temperature for 2.5hr and concentrated *in vacuo*. The residue was dissolved in dichloromethane, washed with saturated sodium bicarbonate solution and dried over magnesium sulfate. The solution was concentrated *in vacuo* to give the title compound.

<Step 4>

N-(2-Chlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid HCl (0.16 g, 0.57 mmol), 1-hydroxybenzotriazole hydrate (0.11 g, 0.85 mmol), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride

(0.16 g, 0.85 mmol) in dichloromethane (30 ml) was added triethylamine (0.12 ml, 1.13 mmol). The reaction mixture was stirred at room temperature for 30min. Then, N-(2-chlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-amino-3(S)-methylpentylamine (0.23 g, 0.57 mmol) was added thereto. The reaction mixture was stirred overnight at room temperature and concentrated *in vacuo*. The residue was dissolved in ethyl acetate, washed with 10% citric acid and saturated sodium bicarbonate solution, and then dried over magnesium sulfate. This solution was concentrated *in vacuo* and the residue was purified by silica gel column chromatography(eluent: CH₂Cl₂/MeOH=40/1, v/v) to give the title compound (0.15 g).

¹H-NMR (CDCl₃) : δ 7.6(d, 2H), 7.4 (m&s, 2H), 7.2(m, 3H), 7.0-7.1(m, 4H), 7.0(s, 1H), 6.8(d, 2H), 5.2(d, 2H), 4.8(dd, 2H), 4.1(m, 1H), 3.7(s, 3H), 3.3(s, 2H), 3.1(dd, 2H), 1.0-1.6(m, 3H), 0.9(m, 6H)

Example 808

N-(3-Chlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

<Step 1>

N-(3-chlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Preparative Example 4, but replacing 2,3-dichlorobenzylamine and 1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetic acid hydrochloride with 3-chlorobenzylamine and 1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetic acid hydrochloride, respectively.

TLC : $R_f = 0.3$ (CH_2Cl_2 / $\text{MeOH} = 10 / 1$)

$^1\text{H-NMR}$ (CDCl_3) : δ 7.6(d, 2H), 7.5(s, 1H), 7.2-7.3(m, 3H), 7.1(m, 3H), 7.0(s, 1H), 5.3(s, 2H), 3.9(m, 1H), 3.7(d, 2H), 3.4(s, 2H), 2.7(d, 2H), 1.0-1.5(m, 3H), 0.8-1.0(m, 6H)

<Step 2>

N-(3-Chlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of N-(3-chlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine (0.50 g, 1.48 mmol) in dichloromethane (10 ml) was added 4-methoxyphenylisothiocyanate (0.20 ml, 1.48 mmol). The reaction mixture was stirred at room temperature for 3hr and concentrated *in vacuo*. The residue was purified by silica gel column chromatography (eluent: n-hexane/ CH_2Cl_2 =2/1, v/v) to give the title compound.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.7(d, 2H), 7.5(s, 1H), 7.3 (m&s, 3H), 7.2(s, 1H), 7.1-7.2(m, 4H), 7.0(s, 1H), 6.8(d, 2H), 5.2(m, 2H), 4.8(dd, 2H), 4.2(m, 1H), 3.8(s, 3H), 3.4(s, 2H), 3.2(dd, 2H), 1.0-1.6(m, 3H), 0.9(m, 6H)

Examples 809-819

N-(3-Chlorobenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 808 to give the title compounds.

Example 809

N-(3-Chlorobenzyl)-N-benzylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

dazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.90-7.62(m, 15H), 6.20 (t, 1H), 5.28(d, 2H), 4.42-5.20(m, 5H), 4.15(m, 1H), 3.25(s, 2H), 3.12(dd, 1H), 1.30-1.65(m, 2H), 1.05(m, 1H), 0.88(m, 6H)

Example 810

N-(3-Chlorobenzyl)-N-(2-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 7.00-7.70(m, 14H), 5.35(s, 2H), 5.18(m, 1H), 4.65-5.02(dd, 2H), 4.24(m, 1H), 3.35(s, 2H), 3.20(dd, 1H), 1.35-1.70(m, 2H), 1.05(m, 1H), 0.90(m, 6H)

Example 811

N-(3-Chlorobenzyl)-N-(3-bromophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.90-7.58(m, 14H), 5.22(s, 2H), 4.90 (t, 1H), 4.30 & 5.22(dd, 2H), 4.15(m, 1H), 3.32(s, 2H), 3.16(dd, 1H), 1.35-1.70(m, 2H), 1.05(m, 1H), 0.90(m, 6H)

Example 812

N-(3-Chlorobenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.95-7.60(m, 14H), 5.22(d, 2H), 4.95 (t, 1H), 4.52 & 5.18(dd, 2H), 4.16(m, 1H), 3.30(s, 2H), 3.18(dd, 1H), 1.35-1.70(m, 2H), 1.05(m, 1H), 0.92(m, 6H)

Example 813

N-(3-Chlorobenzyl)-N-ethylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-7.65(m, 10H), 5.85 (t, 1H), 5.35(d, 2H), 5.04 (t, 1H), 4.42 & 4.68(dd, 2H), 4.10(m, 1H), 3.55(m, 2H), 3.28(s, 2H), 3.08(dd, 1H), 1.35-1.70(m, 2H), 1.05(m, 1H), 1.04 (t, 3H), 0.88(m, 6H)

Example 814

N-(3-Chlorobenzyl)-N-(2-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-7.78(m, 14H), 5.25(s, 2H), 4.15(m, 1H), 4.60 & 5.10(dd, 2H), 4.20(m, 1H), 3.35(s, 2H), 3.16(dd, 1H), 1.35-1.70(m, 2H), 1.05(m, 1H), 0.90(m, 6H)

Example 815

N-(3-Chlorobenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 6.90-7.60(m, 14H), 5.25(s, 2H), 4.95 (bs, 1H), 4.50 & 5.20(dd, 2H), 4.18(m, 1H), 3.35(s, 2H), 3.18(dd, 1H), 1.35-1.70(m, 2H), 1.05(m, 1H), 0.90(m, 6H)

Example 816

N-(3-Chlorobenzyl)-N-(4-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

$^1\text{H-NMR}$ (CDCl_3) : δ 7.00-7.60(m, 14H), 5.25(d, 2H), 4.95-5.18(m, 2H),

4.55(d, 1H), 4.15(m, 1H), 3.32(s, 2H), 3.16(dd, 1H), 1.30-1.70(m, 2H), 1.05(m, 1H), 0.90(m, 6H)

Example 817

N-(3-Chlorobenzyl)-N-methylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.88-7.68(m, 10H), 6.25 (bs, 1H), 5.35(dd, 2H), 5.02(m, 1H), 4.40 & 4.72(dd, 2H), 4.10(m, 1H), 3.30(s, 2H), 3.05(m, 4H), 1.30-1.70(m, 2H), 1.05(m, 1H), 0.92(m, 6H)

Example 818

N-(3-Chlorobenzyl)-N-(3-trifluoromethylphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.95-7.60(m, 14H), 5.22(s, 2H), 4.82 (bs, 1H), 4.50 & 5.38(dd, 2H), 4.18(m, 1H), 3.35(s, 2H), 3.20(dd, 1H), 1.30-1.70(m, 2H), 1.05(m, 1H), 0.90(m, 6H)

Example 819

N-(3-Chlorobenzyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR (CDCl₃) : δ 6.95-7.65(m, 10H), 5.95 (t, 1H), 5.78(m, 1H), 5.20(m, 1H), 5.05(d, 2H), 4.40-4.75(dd, 2H), 4.02-3.35(m, 3H), 1.30-1.70(m, 2H), 1.05(m, 1H), 0.88(m, 6H)

Example 820

N-(2,6-Dichlorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 2,6-dichlorobenzylamine.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.7(d, 2H), 7.4-7.5 (m&s, 2H), 7.3(m, 3H), 7.1-7.2(m, 4H), 6.8(d, 2H), 5.4(m, 2H), 4.9(dd, 2H), 4.3(m, 1H), 3.8(s, 3H), 3.4(s, 2H), 3.2(dd, 2H), 1.0-1.8(m, 3H), 0.9(m, 6H)

Example 821

N-(2-Fluorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 2-fluorobenzylamine.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.7(d, 2H), 7.5 (m&s, 2H), 7.1-7.4(m, 8H), 7.1(s, 4H), 6.9(d, 2H), 5.4(d, 2H), 4.8(dd, 2H), 4.2(m, 1H), 3.8(s, 3H), 3.4(s, 2H), 3.2(dd, 2H), 1.0-1.8(m, 3H), 0.9(m, 6H)

Example 822

N-(2,3-Difluorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 2,3-difluorobenzylamine.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.6(d, 2H), 7.5(s, 2H), 7.4(m, 1H), 7.3(s, 1H),

7.0-7.2(m, 6H), 6.8(d, 2H), 5.3(d, 2H), 4.8(dd, 2H), 4.2(m, 1H), 3.8(s, 3H), 3.4(s, 2H), 3.2(dd, 2H), 1.0-1.8(m, 3H), 0.8(m, 6H)

Example 823

N-(2,6-Difluorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 2,6-difluorobenzylamine.

¹H-NMR (CDCl₃) : δ 7.7(d, 2H), 7.5(s, 2H), 7.3-7.4 (m&s, 1H), 7.1-7.3(m, 5H), 7.1(s, 1H), 6.8(d, 2H), 5.3(d, 2H), 4.9(dd, 2H), 4.3(m, 1H), 3.8(s, 3H), 3.5(s, 2H), 3.3(dd, 2H), 1.0-1.7(m, 3H), 0.9(m, 6H)

Example 824

N-(4-*t*-Butylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 4-*t*-butylbenzylamine.

¹H-NMR (CDCl₃) : δ 7.6(d, 2H), 7.5(s, 1H), 7.4(m, 2H), 7.3(s, 1H), 7.3(m, 4H), 7.1(m, 2H), 6.9(d, 2H), 5.3(d, 2H), 4.8(dd, 2H), 4.3(m, 1H), 3.8(s, 3H), 3.4(s, 2H), 3.2(dd, 2H), 1.4(s, 9H), 1.0-1.7(m, 3H), 0.9(m, 6H)

Example 825

N-(2-Ethoxybenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanoben

zyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 2-ethoxybenzylamine.

Example 826

N-(Pyridin-3-yl)methyl-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 3-amino-methylpyridine.

¹H-NMR (CDCl₃) : δ 8.6(d, 1H), 8.5(s, 1H), 8.1(m, 1H), 7.6(d, 2H), 7.5(s, 1H), 7.3(m, 2H), 7.1-7.2(m, 3H), 7.0(s, 1H), 6.9(d, 2H), 5.3(d, 2H), 4.6(d, 2H), 4.2(m, 1H), 3.8(s, 3H), 3.4(s, 2H), 3.2(dd, 2H), 1.0-1.9(m, 3H), 0.9-1.0(m, 6H)

Example 827

N-[2-(3,4-Dimethoxyphenyl)]ethyl-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 3,4-dimethoxyphenylethylamine.

¹H-NMR (CDCl₃) : δ 7.6(d, 2H), 7.5(s, 1H), 7.3(m, 2H), 7.1(d, 2H), 7.0(m, 2H), 6.8(d, 2H), 6.7(d, 2H), 5.3(d, 2H), 5.1(m, 2H), 4.2(m, 1H), 3.9(s, 6H), 3.8(s, 3H), 3.6(m, 2H), 3.3(s, 2H), 2.9(m, 2H), 1.0-1.7(m,

3H), 0.9-1.0(m, 6H)

Example 828

N-(2-Phenylpropyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 1-amino-2-phenylpropane.

¹H-NMR (CDCl₃) : δ 7.6(d, 2H), 7.5(s, 1H), 7.2-7.4(m, 5H), 7.1-7.2(m, 3H), 7.0(s, 1H), 6.9(m, 1H), 6.8(d, 2H), 5.3(m, 2H), 4.6(m, 1H), 4.2(m, 1H), 3.9(s, 3H), 3.8(s, 2H), 3.3(m, 4H), 2.0-2.7(m, 3H), 2.4(m, 3H), 1.0(m, 6H), 0.8(d, 3H)

Example 829

N-[2-(2-methoxyphenyl)ethyl]-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 2-(2-methoxyphenyl)ethylamine.

¹H-NMR (CDCl₃) : δ 7.6(d, 2H), 7.5(m, 2H), 7.2-7.3(m, 3H), 7.2(d, 1H), 7.1(d, 2H), 6.9-7.0(m, 4H), 5.3(m, 2H), 4.2(m, 1H), 3.9(s, 3H), 3.7(s, 3H), 3.6 (q, 2H), 3.3(s, 2H), 3.2(d, 2H), 2.9(m, 2H), 1.1-1.7(m, 3H), 0.9(m, 6H)

Example 830

N-(4-Nitrobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenz

yl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 4-nitrobenzylamine.

¹H-NMR (CDCl₃) : δ 8.16-8.21(m, 2H), 7.96 (bs, 1H), 7.55-7.60(m, 2H), 7.47(s, 1H), 7.36-7.43(m, 2H), 7.00-7.17(m, 5H), 6.82-6.88(m, 3H), 6.57-6.03(m, 1H), 5.20-5.38(m, 3H), 4.84-5.03(m, 1H), 4.59-4.71(m, 1H), 4.04-4.16(m, 1H), 3.79(s, 3H), 3.35(m, 2H), 3.12(m, 1H), 1.54-1.63(m, 1H), 1.35(m, 1H), 1.12(m, 1H), 0.90(m, 6H)

Example 831

N-[2-(2-Fluorophenyl)]ethyl-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 2-(2-fluorophenyl)ethylamine.

¹H-NMR (CDCl₃) : δ 7.60(m, 3H), 7.43(s, 1H), 7.14-7.21(m, 5H), 7.08(m, 4H), 6.99(m, 1H), 5.26(m, 2H), 5.00(m, 1H), 4.14(m, 1H), 3.81(s, 3H), 3.42-3.58(m, 1H), 3.28(s, 2H), 3.02-3.15(m, 1H), 2.94 (bs, 2H), 1.65(m, 1H), 1.45(m, 1H), 1.10(m, 1H), 0.93(m, 6H)

Example 832

N-(4-methoxybenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure

as Example 807, but replacing 2-chlorobenzylamine with 4-methoxybenzylamine.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.60(d, 2H), 7.47(s, 1H), 7.29-7.35(m, 2H), 7.09-7.17(m, 4H), 7.02(m, 3H), 7.00(s, 1H), 6.85(m, 3H), 5.14-5.38(m, 3H), 4.52-4.82(m, 2H), 4.15(m, 1H), 3.80(s, 3H), 3.78(s, 3H), 3.32(s, 2H), 3.11-3.22(m, 1H), 1.59-1.63(m, 1H), 1.43-1.51(m, 1H), 1.12(m, 1H), 0.90(m, 6H)

Example 833

N-(3,4-Methylenedioxybenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with piperonylamine.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.60(d, 2H), 7.20-7.50(m, 3H), 7.00-7.18(m, 4H), 6.60-6.90(m, 4H), 6.04(s, 2H), 5.10-5.35(m, 3H), 4.52-4.82(m, 2H), 4.11-4.21(m, 1H), 3.80(s, 3H), 3.32(s, 2H), 3.11-3.22(m, 1H), 2.02(m, 1H), 1.40-1.63(m, 2H), 1.02-1.15(m, 2H), 0.92(m, 6H)

Example 834

N-(2-Methylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 2-methylbenzylamine.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.6(d, 2H), 7.4(s, 1H), 7.2(m, 2H), 7.1(m, 3H),

7.0(s, 2H), 6.8(d, 2H), 5.3(m, 2H), 4.5-4.8(dd, 2H), 4.2(m, 1H), 3.8(s, 3H), 3.3(s, 2H), 3.1(dd, 2H), 2.3(s, 3H), 1.1-1.5(m, 3H), 0.9(m, 6H)

Example 835

N-(2-Methylbenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine and 4-methoxyphenylisothiocyanate with 2-methylbenzylamine and 3-fluorophenylisothiocyanate, respectively.

¹H-NMR (CDCl₃) : δ 7.6(d, 2H), 7.4(s, 1H), 7.2-7.3(m, 3H), 7.1(m, 3H), 7.0(s, 2H), 6.9(d, 2H), 5.3(m, 2H), 4.8(dd, 2H), 4.2(m, 1H), 3.4(s, 2H), 3.1(d, 2H), 2.3(s, 3H), 1.1-1.6(m, 3H), 0.9-1.0(m, 6H)

Example 836

N-(2-Methylbenzyl)-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine and 4-methoxyphenylisothiocyanate with 2-methylbenzylamine and 2-methoxypyridin-5-ylisothiocyanate, respectively.

¹H-NMR (CDCl₃) : δ 7.8(s, 1H), 7.6(d, 2H), 7.4(m, 1H), 7.3(s, 1H), 7.2(m, 3H), 7.1 (s+d, 3H), 7.0(s, 1H), 6.7(d, 1H), 5.3(d, 2H), 4.5 & 5.0(dd, 2H), 4.2(m, 1H), 3.8(s, 3H), 3.3(s, 2H), 3.1(d, 2H), 2.4(s, 3H), 1.0-1.6(m, 3H), 0.8-0.9(m, 6H)

Example 837

N-(4-Fluorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 4-fluorobenzylamine.

¹H-NMR (CDCl₃) : δ 7.6(d, 2H), 7.4(s, 1H), 7.3(m, 1H), 7.2(m, 2H), 7.0-7.1(m, 5H), 7.0(s, 1H), 6.8(d, 2H), 5.3(m, 2H), 4.5-4.8(dd, 2H), 4.1-4.2(m, 1H), 3.8(s, 3H), 3.3(s, 2H), 3.1(dd, 2H), 1.1-1.5(m, 3H), 0.9(m, 6H)

Example 838

N-(Pyridin-4-ylmethyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 4-aminomethylpyridine.

¹H-NMR (CDCl₃) : δ 8.5(d, 2H), 7.6(d, 2H), 7.6(s, 1H), 7.5(m, 1H), 7.0-7.1(m, 5H), 6.9(s, 1H), 6.8(d, 2H), 5.2(s, 2H), 4.5-4.8(dd, 2H), 4.1-4.2(m, 1H), 3.8(s, 3H), 3.3(s, 2H), 3.1(dd, 2H), 1.1-1.5(m, 3H), 0.9(m, 6H)

Example 839

N-(Pyridin-2-ylmethyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 2-aminomethylpyridine.

¹H-NMR (CDCl₃) : δ 8.6(d, 2H), 7.8(m, 2H), 7.6(s, 1H), 7.5(s, 1H), 7.3-7.4(m, 3H), 7.1(d, 2H), 7.0(s, 1H), 6.9(d, 2H), 5.3(d, 2H), 4.4-4.8(dd, 2H), 4.2(m, 1H), 3.8(s, 3H), 3.3(s, 2H), 3.1(dd, 2H), 1.0-1.6(m, 3H), 0.9(m, 6H)

Example 840

N-(Pyridin-2-ylmethyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine and 4-methoxyphenylisothiocyanate with 2-aminomethylpyridine and 3-fluorophenylisothiocyanate, respectively.

¹H-NMR (CDCl₃) : δ 8.6(d, 1H), 7.8 (t, 1H), 7.6(d, 2H), 7.5 (m+s, 2H), 7.2-7.4(m, 4H), 7.2(d, 2H), 7.0(s, 1H), 6.9 (t, 1H), 5.3(s, 2H), 4.4 & 4.9(dd, 2H), 4.3(m, 1H), 3.3(m, 2H), 3.1(dd, 2H), 1.1-1.6(m, 3H), 0.9(m, 6H)

Example 841

N-(3-Fluorobenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 3-fluorobenzylamine.

¹H-NMR (CDCl₃) : δ 7.7(d, 2H), 7.5(s, 2H), 7.4(m, 1H), 7.3(d, 1H), 7.1-7.2(m, 7H), 6.9(d, 2H), 5.4(s, 2H), 4.9(dd, 2H), 4.3(m, 1H), 3.9(s, 3H), 3.4(s, 2H), 3.3(dd, 2H), 1.2-1.7(m, 3H), 1.0(m, 6H)

Example 842

N-(3-Fluorobenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine and 4-methoxyphenylisothiocyanate with 3-fluorobenzylamine and 3-fluorophenylisothiocyanate, respectively.

¹H-NMR (CDCl₃) : δ 7.6(d, 2H), 7.4(s, 1H), 7.2-7.3(m, 2H), 6.8-7.1(m, 9H), 5.2(s, 2H), 4.5 & 5.1(dd, 2H), 4.1(m, 1H), 3.3(s, 2H), 3.2(dd, 2H), 1.1-1.6(m, 3H), 0.9(m, 6H)

Example 843

N-(3-Fluorobenzyl)-N-cyclohexylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine and 4-methoxyphenylisothiocyanate with 3-fluorobenzylamine and cyclohexylisothiocyanate, respectively.

¹H-NMR (CDCl₃) : δ 7.7(d, 2H), 7.4-7.5(m, 3H), 7.3-7.4(m, 2H), 7.2(d, 2H), 7.0(s, 1H), 5.3(d, 2H), 5.1-5.2(m, 1H), 4.5-4.8(m, 2H), 4.2(m, 1H), 3.3(s, 2H), 3.1(dd, 2H), 1.8-2.0(m, 2H), 1.3-1.6(m, 6H), 1.0-1.2(m, 3H),

0.8-1.0(m, 8H)

Example 844

N-(3-Fluorobenzyl)-N-(2-methoxypyridin-5-yl)thiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine and 4-methoxyphenylisothiocyanate with 3-fluorobenzylamine and 2-methoxypyridin-5-ylisothiocyanate, respectively.

¹H-NMR (CDCl₃) : δ 7.8(d, 1H), 7.5-7.6(m, 7H), 7.4(s, 1H), 7.1(d, 2H), 7.0(s, 1H), 6.7(m, 1H), 4.6 & 5.2(s, 2H), 4.2(m, 1H), 3.9(s, 3H), 3.3(s, 2H), 3.2(dd, 2H), 1.0-1.6(m, 3H), 0.8-0.9(m, 6H)

Example 845

N-(3-Trifluoromethylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 3-trifluoromethylbenzylamine.

¹H-NMR (CDCl₃) : δ 7.7(d, 2H), 7.6(m, 2H), 7.5(s, 1H), 7.3(d, 1H), 7.1-7.2(m, 5H), 7.1(s, 1H), 6.9(d, 2H), 5.3(s, 2H), 5.0(dd, 2H), 4.3(m, 1H), 3.9(s, 3H), 3.4(s, 2H), 3.3(dd, 2H), 1.2-1.7(m, 3H), 0.9(m, 6H)

Example 846

N-(3-Trifluoromethylbenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine and 4-methoxyphenylisothiocyanate with 3-trifluoromethylbenzylamine and 3-fluorophenylisothiocyanate, respectively.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.5-7.7(m, 5H), 7.5(s, 1H), 7.3(m, 1H), 6.8-7.2(m, 7H), 5.3(s, 2H), 4.6 & 5.1(dd, 2H), 4.2(m, 1H), 3.4(s, 2H), 3.2(dd, 2H), 1.1-1.6(m, 3H), 0.9-1.0(m, 6H)

Example 847

N-(3-Trifluoromethylbenzyl)-N-cyclohexylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine and 4-methoxyphenylisothiocyanate with 3-trifluoromethylbenzylamine and cyclohexylisothiocyanate, respectively.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.7(d, 2H), 7.5(s, 1H), 7.2-7.3(m, 2H), 7.2(d, 2H), 6.8-7.0(m, 3H), 5.3(s, 2H), 5.2(m, 1H), 4.5 & 4.8(m, 2H), 4.1(m, 1H), 3.3(s, 2H), 3.1(dd, 2H), 1.8-2.0(m, 2H), 1.3-1.6(m, 6H), 1.0-1.2(m, 3H), 0.8-0.9(m, 6H)

Example 848

N-(3-Trifluoromethylbenzyl)-N-(2-methoxypyridin-5-ylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine and 4-methoxyphenyl-

isothiocyanate with 3-trifluoromethylbenzylamine and 2-methoxypyridin-5-ylisothiocyanate, respectively.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.8(d, 1H), 7.6(d, 2H), 7.5(d, 1H), 7.3 (m+s, 2H), 6.9-7.1 (d+m, 4H), 6.7(d, 1H), 5.2(d, 2H), 4.5 & 5.2(dd, 2H), 4.2(m, 1H), 3.8(s, 3H), 3.3(s, 2H), 3.2(dd, 2H), 1.0-1.6(m, 3H), 0.8-0.9(m, 6H)

Example 849

N-(3-Methoxycarbonylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 3-methoxycarbonylbenzylamine.

$^1\text{H-NMR}$ (CDCl_3) : δ 7.99(d, 1H), 7.89(s, 1H), 7.58(d, 2H), 7.44(m, 3H), 7.02-7.11(m, 5H), 6.82(d, 2H), 5.27(m, 2H), 5.16(m, 2H), 4.63(d, 1H), 4.06-4.23(m, 1H), 3.92(s, 3H), 3.78(s, 3H), 3.40(s, 2H), 3.13-3.21(m, 1H), 1.52-1.65(m, 1H), 1.38(m, 1H), 1.02(m, 1H), 0.90(m, 6H)

Example 850

N-(3-Methoxycarbonylbenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine and 4-methoxyphenylisothiocyanate with 3-methoxycarbonylbenzylamine and 3-fluorophenylisothiocyanate, respectively.

$^1\text{H-NMR}$ (CDCl_3) : δ 8.01(d, 1H), 7.90(s, 1H), 7.59(d, 2H), 7.46(m, 3H),

7.19-7.26(m, 1H), 6.86-7.11(m, 7H), 5.18-5.30(m, 3H), 4.95(m, 1H), 4.60(d, 1H), 4.10-4.23(m, 1H), 3.93(s, 3H), 3.35(s, 2H), 3.24(m, 1H), 1.70(m, 1H), 1.43-1.60(m, 1H), 1.06(m, 1H), 0.90(m, 6H)

Example 851

N-(3-Carboxybenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine hydrochloride

To a solution of the compound of Example 850 (110 mg) in ethanol(1.5 ml) was added lithium hydroxide solution (1M, 2 ml). The reaction mixture was stirred at room temperature for 3hr. After the addition of 1N HCl solution (2.5 ml), the mixture was extracted with dichloromethane. The organic phase was dried over magnesium sulfate and concentrated *in vacuo* to give a white solid of the title compound (57 mg, 53%).

¹H-NMR (CDCl₃) : δ 9.54(d, 1H), 8.94(s, 1H), 8.30-8.47(m, 1H), 7.93(m, 4H), 7.42-7.85(m, 4H), 7.15-7.38(m, 3H), 7.00 (t, 1H), 5.60(s, 2H), 5.13-5.40(m, 2H), 4.40(m, 1H), 4.05(m, 1H), 3.39-3.76(m, 3H), 1.40-1.52(m, 2H), 1.19-1.30(m, 1H), 0.86(m, 6H)

Example 852

N-(4-Methoxycarbonylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 4-methoxycarbonylbenzylamine.

¹H-NMR (CDCl₃) : δ 8.02(d, 2H), 7.59(d, 2H), 7.49(s, 1H), 7.30(m, 2H),

7.06-7.12(m, 4H), 7.02(s, 1H), 6.83(d, 2H), 5.30(m, 2H), 5.16(m, 2H), 4.65(d, 1H), 4.03-4.27(m, 1H), 3.92(s, 3H), 3.78(s, 3H), 3.33(s, 2H), 3.12(m, 1H), 1.63(m, 1H), 1.40(m, 1H), 1.05(m, 1H), 0.90(m, 6H)

Example 853

N-(4-Methoxycarbonylbenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine and 4-methoxyphenylisothiocyanate with 4-methoxycarbonylbenzylamine and 3-fluorophenylisothiocyanate, respectively.

¹H-NMR (CDCl₃) : δ 9.25(s, 2H), 8.50(m, 1H), 8.00(m, 4H), 7.69(s, 1H), 7.53(d, 2H), 7.40(d, 2H), 7.16(d, 2H), 6.90(m, 2H), 5.64(s, 2H), 5.20(m, 2H), 4.23-5.54(m, 1H), 4.05(m, 1H), 3.81(s, 3H), 3.40-3.73(m, 2H), 1.51 (bs, 2H), 1.25(m, 1H), 0.90(m, 6H)

Example 854

N-(4-Carboxybenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine hydrochloride

The title compound was prepared according to the same procedure as Example 851, but replacing the compound of Example 850 with the compound of Example 852.

¹H-NMR (CDCl₃) : δ 9.25(s, 1H), 8.41-8.61(m, 1H), 7.95(m, 4H), 7.69(s, 1H), 7.53(m, 4H), 7.15(d, 2H), 6.90(d, 2H), 5.64(s, 2H), 5.16-5.29(m, 2H), 4.37(m, 1H), 3.98(m, 1H), 3.81(m, 3H), 3.43-3.69(m, 3H), 1.50-1.58(m, 2H), 1.12(m, 1H), 0.88(m, 6H)

Example 855

N-(4-Carboxybenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine hydrochloride

The title compound was prepared according to the same procedure as Example 851, but replacing the compound of Example 850 with the compound of Example 853.

¹H-NMR (CDCl₃) : δ 9.57 (bs, 1H), 9.26(s, 1H), 8.43-8.63(m, 1H), 8.00(m, 4H), 7.71(s, 1H), 7.53(d, 2H), 7.42(d, 2H), 7.17-7.34(m, 3H), 7.02(m, 1H), 5.66(s, 2H), 5.18-5.42(m, 2H), 4.26-4.50(m, 1H), 4.08(m, 1H), 3.40-3.71(m, 3H), 1.50-1.62(m, 2H), 1.15(m, 1H), 0.87(m, 6H)

Example 856

N-(1-Oxypyridin-2-ylmethyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of the compound of Example 839 (62 mg) in dichloromethane (5 ml) was added *m*-chloroperbenzoic acid (0.04 g). The reaction mixture was stirred for 2hr at room temperature. After concentration *in vacuo*, the residue was purified by column chromatography(eluent: methylene chloride/methanol=9/1, v/v) to give a solid of the title compound.

¹H-NMR (DMSO-d₆ + TFA-d₁) : δ 8.7(s, 1H), 8.2(m, 1H), 7.8(m, 2H), 7.6-7.8(m, 3H), 7.4(d, 2H), 7.2-7.3(m, 3H), 6.9(d, 2H), 5.4(s, 2H), 5.1(m, 2H), 4.1(m, 1H), 3.4-3.7 (m & s, 7H), 1.4(m, 2H), 1.0(m, 1H), 0.8(m, 6H)

Example 857

N-Methyl-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with methylamine.

¹H-NMR (CDCl₃) : δ 7.40-7.70(m, 3H), 7.30(s, 1H), 7.00-7.25(m, 5H), 6.80-6.95(m, 2H), 5.00-5.40(m, 3H), 4.00-4.30(m, 1H), 3.80(m, 4H), 3.30(m, 2H), 3.18(s, 3H), 3.07(dd, 1H), 1.37-1.80(m, 2H), 1.00-1.30(m, 1H), 0.92(m, 6H)

Example 858

N-Isobutyl-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with isobutylamine.

¹H-NMR (CDCl₃) : δ 7.60(d, 2H), 7.35-7.53(m, 2H), 7.00-7.25(m, 5H), 6.80-6.93(m, 2H), 5.10-5.40(m, 3H), 4.00-4.30(m, 1H), 3.80(m, 3H), 3.40-3.70(m, 2H), 3.27(s, 3H), 2.95-3.20(m, 2H), 1.30-2.40(m, 3H), 0.80-1.30(m, 13H)

Example 859

N-n-Butyl-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with n-butylamine.

¹H-NMR (CDCl₃) : δ 7.6(d, 2H), 7.5(s, 1H), 7.2(d, 2H), 7.1(d, 2H), 7.0(s, 1H), 6.9(d, 2H), 5.2-5.3(m, 2H), 4.1(m, 1H), 3.8(s, 3H), 3.4-3.7(m, 2H), 3.3(s, 2H), 3.0-3.2(m, 2H), 1.5-1.7(m, 5H), 1.1-1.4(m, 5H), 0.9(m, 6H)

Example 860

N-[2-(Ethylthio)ethyl]-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 2-(ethylthio)ethylamine.

¹H-NMR (CDCl₃) : δ 7.6(d, 2H), 7.4(s, 1H), 7.2(d, 2H), 7.1(d, 2H), 7.0(s, 1H), 6.8(d, 2H), 5.3(s, 2H), 4.1(m, 1H), 3.8(s, 3H), 3.4-3.6(m, 2H), 3.3(s, 2H), 3.2(dd, 2H), 2.8 (t, 2H), 2.6 (q, 2H), 1.5-1.6(m, 2H), 1.3 (t, 3H), 1.1(m, 1H), 0.9-1.0(m, 6H)

Example 861

N-(3-Ethoxy)propyl-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with 3-ethoxypropylamine.

¹H-NMR (CDCl₃) : δ 7.6(m, 3H), 7.5(d, 2H), 7.1-7.2(m, 3H), 7.0(s, 1H), 6.9(d, 1H), 5.3(s, 2H), 4.1-4.2(m, 3H), 3.8(s, 3H), 3.4-3.6(m, 4H), 3.3(s, 2H), 3.1(dd, 2H), 1.4-1.8(m, 3H), 1.2 (t, 3H), 0.9-1.0(m, 6H)

Example 862

N-(2-Propynyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine with propargylamine.

¹H-NMR (CDCl₃) : δ 7.57(d, 2H), 7.46(s, 1H), 7.08(d, 2H), 6.92(s, 1H), 6.78(m, 1H), 5.21(s, 2H), 5.05(s, 1H), 4.45(m, 1H), 4.00-4.30(m, 3H), 3.78(s, 3H), 3.35-3.70(m, 1H), 3.29(s, 2H), 2.90-3.25(m, 1H), 1.00-1.90(m, 3H), 0.88(m, 6H)

Example 863

N-(2-Propynyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

The title compound was prepared according to the same procedure as Example 807, but replacing 2-chlorobenzylamine and 4-methoxyphenylisothiocyanate with propargylamine and 3-fluorophenylisothiocyanate, respectively.

¹H-NMR (CDCl₃) : δ 7.58(d, 2H), 7.48(s, 1H), 7.00-7.30(m, 3H), 6.93(s, 1H), 6.67-6.87(m, 1H), 6.40-6.66(m, 3H), 5.20(s, 2H), 5.09(s, 1H), 4.50(m, 1H), 4.00-4.30(m, 3H), 3.35-3.80(m, 1H), 3.29(s, 2H), 2.95-3.25(m, 1H), 1.00-1.90(m, 3H), 0.90(m, 6H)

Example 864

N-(2-Trifluoromethylbenzyl)-N-(allylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

<Step 1>

N-(2-Trifluoromethylbenzyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

Using the same method as described in Preparative Example 3, N-*t*-butoxycarbonyl-L-isoleucine was converted to N-(*t*-butoxycarbonyl)-L-isoleucine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 2,3-dichlorobenzylamine with 2-trifluoromethylbenzylamine to give the title compound.

¹H-NMR(CDCl₃) : δ 8.17(d, 2H), 7.65(d, 1H), 7.52(d, 2H), 7.51(s, 1H), 7.33-7.41(m, 1H), 7.17(d, 2H), 7.04(s, 1H), 5.93(d, 1H), 5.30(s, 2H), 3.89(s, 2H), 3.80-3.87(m, 1H), 3.36(s, 2H), 2.69(d, 2H), 1.44-1.54(m, 1H), 1.33-1.40(m, 1H), 0.95-1.01(m, 1H), 0.80-0.92(m, 6H)

<Step 2>

N-(2-Trifluoromethylbenzyl)-N-(allylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

To a solution of N-(2-Trifluoromethylbenzyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added allylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 2hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: CH₂Cl₂/MeOH=9/1, v/v) to give the title compound as a white solid.

¹H-NMR(CDCl₃) : δ 8.21(d, 2H), 7.72(d, 1H), 7.39-7.53(m, 3H),

7.15-7.28(m, 3H), 7.02(s, 1H), 5.87(bs, 1H), 5.71-5.85(m, 1H), 5.30-5.52(m, 2H), 4.70-5.08(m, 2H), 4.65(d, 1H), 4.21-4.29(m, 2H), 4.05-4.14(m, 1H), 3.33(s, 2H), 3.06(dd, 1H), 1.65(bs, 1H), 1.26-1.44(m, 1H), 0.97-1.05(m, 1H), 0.86-0.92(m, 6H)

Examples 865-868

N-(2-Trifluoromethylbenzyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 864 to give the title compounds.

Example 865

N-(2-Trifluoromethylbenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 8.15(d, 2H), 7.70(d, 1H), 7.40-7.58(m, 3H), 7.19-7.30(m, 5H), 7.14(d, 2H), 6.97(s, 1H), 5.22-5.41(m, 1H), 5.31(d, 2H), 4.82-4.95(m, 1H), 4.77(d, 1H), 3.34(s, 2H), 3.13(dd, 1H), 1.64-1.70(m, 1H), 1.40-1.48(m, 1H), 0.98-1.06(m, 1H), 0.86-0.93(m, 6H)

Example 866

N-(2-Trifluoromethylbenzyl)-N-cyclohexylthiocarbamoyl-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 8.20(d, 2H), 7.70-7.74(m, 1H), 7.55(s, 1H), 7.42-7.46(m, 2H), 7.13-7.26(m, 3H), 7.04(s, 1H), 5.42(d, 2H), 5.17(bs, 1H), 4.73(dd, 2H), 4.17-4.22(m, 1H), 4.05-4.11(m, 1H), 3.34(s, 2H), 3.04(dd, 1H), 1.63-1.90(m, 4H), 1.26-1.50(m, 6H), 0.82-1.20(m, 6H)

Example 867

N-(2-Trifluoromethylbenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 8.28(bs, 1H), 8.14(d, 2H), 7.72(d, 1H), 7.40-7.60(m, 3H), 7.23-7.28(m, 2H), 7.03-7.20(m, 3H), 6.84-7.16(m, 3H), 5.38-5.48(m, 1H), 5.32(s, 2H), 4.82-4.95(m, 1H), 4.77(d, 1H), 4.08-4.16(m, 1H), 3.35(s, 2H), 3.18(dd, 1H), 1.62-1.70(m, 1H), 1.38-1.46(m, 1H), 0.98-1.06(m, 1H), 0.86-0.92(m, 6H)

Example 868

N-(2-Trifluoromethylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-nitrobenzyl)-1H-imidazol-5-yl]acetyl}amino-3(S)-methylpentylamine

¹H-NMR(CDCl₃) : δ 8.15(d, 2H), 7.72(d, 1H), 7.66(bs, 1H), 7.41-7.57(m, 3H), 7.24-7.29(m, 2H), 7.07-7.18(m, 3H), 7.01(s, 1H), 6.84(d, 2H), 5.35(d, 2H), 5.08-5.26(m, 2H), 4.79(d, 1H), 4.06-4.18(m, 1H), 3.78(s, 3H), 3.34(s, 2H), 3.11(dd, 1H), 1.62-1.73(m, 1H), 1.32-1.48(m, 1H), 0.96-1.09(m, 1H), 0.86-0.92(m, 6H)

Example 869

N-(2-Trifluoromethylbenzyl)-N-allylthiocarbamoyl-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

<Step 1>

N-(2-Trifluoromethylbenzyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

Using the same method as described in Preparative Example 3, N-*t*-butoxycarbonyl-L-glycine was converted to N-(*t*-butoxycarbonyl)-L-

glycine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 2,3-dichlorobenzylamine and 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride with 2-trifluoromethylbenzylamine and 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride, respectively, to give the title compound.

¹H-NMR(CDCl₃) : δ 7.32-7.63(m, 7H), 7.14(d, 2H), 7.01(s, 1H), 6.53(bs, 1H), 5.26(s, 2H), 3.89(s, 2H), 3.36(s, 2H), 3.27(q, 2H), 2.73(t, 2H)

<Step 2>

N-(2-Trifluoromethylbenzyl)-N-(allylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]aminoethylamine

To a solution of N-(2-Trifluoromethylbenzyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]aminoethylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added allylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 2hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: CH₂Cl₂/MeOH=9/1, v/v) to give the title compound as a white solid.

¹H-NMR(CDCl₃) : δ 7.64(d, 2H), 7.53(s, 1H), 7.25-7.46(m, 2H), 7.31-7.44(m, 2H), 7.16(d, 2H), 7.06(bs, 1H), 6.98(s, 1H), 6.61(bs, 1H), 5.79-5.99(m, 1H), 5.26(s, 2H), 5.14(s, 2H), 5.08(s, 2H), 4.28-4.33(m, 2H), 3.80(t, 2H), 3.36(s, 2H), 3.27-3.33(m, 2H)

Examples 870-873

N-(2-Trifluoromethylbenzyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]aminoethylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 869 to give the title compounds.

Example 870

N-(2-Trifluoromethylbenzyl)-N-(4-chlorophenylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]aminoethylamine

¹H-NMR(CDCl₃) : δ 8.90(bs, 1H), 7.68(d, 1H), 7.51-7.61(m, 4H), 7.40-7.47(m, 3H), 7.29(d, 2H), 7.06(d, 2H), 6.99(bs, 1H), 6.93(s, 1H), 5.31(s, 2H), 5.18(s, 2H), 3.68(t, 2H), 3.37(s, 2H), 3.29-3.34(m, 2H)

Example 871

N-(2-Trifluoromethylbenzyl)-N-cyclohexylthiocarbamoyl-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]aminoethylamine

¹H-NMR(CDCl₃) : δ 7.69(d, 1H), 7.63(d, 2H), 7.53(s, 1H), 7.40-7.49(m, 2H), 7.29(d, 1H), 7.16(d, 2H), 7.00(s, 1H), 6.06(bs, 1H), 5.29(s, 2H), 5.01(s, 2H), 4.23-4.30(m, 1H), 3.85(t, 2H), 3.37(s, 2H), 3.27-3.33(m, 2H), 1.90-1.97(m, 2H), 1.44-1.62(m, 2H), 0.99-1.39(m, 6H)

Example 872

N-(2-Trifluoromethylbenzyl)-N-(3-fluorophenylthiocarbamoyl)-2-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl]aminoethylamine

¹H-NMR(CDCl₃) : δ 8.82(bs, 1H), 7.69(d, 1H), 7.59(s, 1H), 7.54(s, 2H), 7.38-7.49(m, 2H), 7.23-7.33(m, 3H), 7.09(d, 2H), 6.99(s, 1H), 6.86-6.96(m, 1H), 6.66(bs, 1H), 5.32(s, 2H), 5.21(s, 2H), 3.72(t, 2H), 3.39(s, 2H), 3.27-3.34(m, 2H)

Example 873

N-(2-Trifluoromethylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}aminoethylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.42(bs, 1H), 7.68(d, 1H), 7.56(d, 2H), 7.38-7.50(m, 3H), 7.26(d, 2H), 6.97(d, 2H), 6.95(s, 1H), 6.87(d, 2H), 5.25(s, 2H), 5.20(s, 2H), 3.80-(bs, 5H), 3.36(bs, 2H)

Example 874

N-(2-Trifluoromethylbenzyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

<Step 1>

N-(2-Trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

Using the same method as described in Preparative Example 3, N-*t*-butoxycarbonyl-L-(O-benzyl)tyrosine was converted to N-*t*-butoxycarbonyl-L-(O-benzyl)tyrosine aldehyde. And then the reaction was carried out under the same condition as described in Preparative Example 4, but replacing 2,3-dichlorobenzylamine and 1-(4-nitrobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride with 2-trifluoromethylbenzylamine and 1-(4-cyanobenzyl)-1H-imidazol-5-ylacetic acid hydrochloride, respectively, to give the title compound.

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.62(d, 1H), 7.58(d, 2H), 7.51-7.54(m, 2H), 7.30-7.45(m, 7H), 6.96-7.03(m, 5H), 6.84(d, 2H), 6.12(d, 1H), 5.03(s, 2H), 4.86(d, 1H), 4.17-4.22(m, 1H), 3.86(s, 2H), 3.26(t, 2H), 2.62-2.71(m, 4H)

<Step 2>

N-(2-Trifluoromethylbenzyl)-N-allylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine

To a solution of N-(2-trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine in dichloromethane (0.02M, 1ml, 0.02mmol) was added allylisothiocyanate (0.1M in CH₂Cl₂, 0.2ml, 0.02mmol). The reaction mixture was agitated for 2hr at room temperature. The mixture was purified by silica gel column chromatography(eluent: CH₂Cl₂/MeOH=9/1, v/v) to give the title compound as a white solid.

¹H-NMR(CDCl₃) : δ 7.70(d, 1H), 7.60(d, 2H), 7.42(m, 5H), 7.32(m, 5H), 7.00(m, 7H), 6.68(s, 1H), 5.82(m, 1H), 5.32(d, 1H), 5.07(m, 4H), 4.73(m, 4H), 4.31(m, 3H), 3.50(t, 1H), 3.33(m, 1H), 3.12(m, 1H), 2.85(m, 1H), 2.65(m, 1H)

Examples 875-878

N-(2-Trifluoromethylbenzyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxy)phenylpropylamine was reacted with the corresponding isothiocyanates under the same condition as described in <Step 2> of Example 874 to give the title compounds.

Example 875

N-(2-Trifluoromethylbenzyl)-N-(4-chlorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxyphenyl)propylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.70(bs, 1H), 7.71(d, 2H), 7.55(d, 3H), 7.35(m, 12H), 6.95(m, 6H), 6.30(bs, 1H), 5.80(d, 1H), 5.07(s, 2H), 4.85(d, 1H), 4.65(q, 2H), 4.47(m, 1H), 4.20(m, 1H), 3.48(t, 1H), 3.33(m, 1H), 3.16(m, 1H), 2.95(m, 1H), 2.60(m, 1H)

Example 876

N-(2-Trifluoromethylbenzyl)-N-cyclohexylthiocarbamoyl-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxyphenyl)propylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 7.70(d, 1H), 7.58(d, 3H), 7.40(m, 7H), 7.18(d, 2H), 7.00(m, 5H), 6.85(m, 3H), 5.82(bs, 1H), 5.07(s, 2H), 4.80(m, 3H), 4.65(d, 1H), 4.20(m, 2H), 3.48(t, 1H), 3.33(m, 1H), 3.10(m, 1H), 2.75(m, 2H), 1.90(m, 2H), 1.55(m, 4H), 1.00(m, 4H)

Example 877

N-(2-Trifluoromethylbenzyl)-N-(3-fluorophenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxyphenyl)propylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.80(bs, 1H), 7.70(d, 1H), 7.55(d, 3H), 7.37(m, 4H), 7.28(m, 7H), 6.96(m, 8H), 6.30(bs, 1H), 5.80(d, 1H), 5.07(s, 2H), 4.85(d, 1H), 4.65(q, 2H), 4.50(m, 1H), 4.20(m, 1H), 3.48(t, 1H), 3.30(m, 1H), 3.16(m, 1H), 2.95(m, 1H), 2.60(m, 1H)

Example 878

N-(2-Trifluoromethylbenzyl)-N-(4-methoxyphenylthiocarbamoyl)-2(S)-{[1-(4-cyanobenzyl)-1H-imidazol-5-yl]acetyl}amino-3-(4-benzyloxyphenyl)propylamine

$^1\text{H-NMR}(\text{CDCl}_3)$: δ 8.10(bs, 1H), 7.70(d, 1H), 7.55(d, 3H), 7.40(m,

6H), 7.30(m, 2H), 7.20(d, 2H), 6.96(m, 9H), 6.60(bs, 1H), 5.60(d, 1H), 5.07(s, 2H), 4.74(m, 4H), 4.30(m, 1H), 3.80(s, 3H), 3.48(t, 1H), 3.34(m, 1H), 3.16(m, 1H), 2.90(m, 1H), 2.60(m, 1H)

Experimental Example 1

In Vitro Cell Growth Inhibition Assay

The viability of K-ras transformed cells was measured by using MTT colorimetric assay which is based on the conversion of MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) to MTT-formazan by mitochondrial enzyme. In brief, cells were dispensed within 96-well culture plate in 100 μ l culture medium at a density of 200 cells/well. Following 24 hours incubation at 37°C, 5% CO₂, 100% relative humidity, 100 μ l of culture medium containing compound or culture medium containing compound vehicle was dispensed within appropriate wells. Culture plates were then incubated for 4 days prior to addition of MTT reagent. MTT solution (5 mg/ml PBS) was added to the well in a concentration of 0.5 mg/ml. After incubation for 4 hours, mixed culture medium and MTT solution were carefully removed, then 100 μ l DMSO was added to the well to solubilize formazan. The absorbance of each well was measured using microculture plate reader at 570 nm. Measurements were performed in triplicate. Growth inhibition of 50% (IC₅₀) is calculated in terms of %T/C [(absorbance of treated cells/absorbance of control cells) \times 100]. The results of effective compounds shown in Table 1 reflects their ability to inhibit K-ras transformed cell growth *in vitro*.

Table 1. Inhibition of K-ras transformed cell growth

Compound	IC ₅₀ (μM)	Compound	IC ₅₀ (μM)
Example 1	4.1	Example 2	1.0
Example 3	1.0	Example 4	1.3
Example 5	2.6	Example 6	3.4
Example 7	1.1	Example 8	1.1
Example 9	0.7	Example 10	5.6
Example 11	3.7	Example 12	2.1
Example 13	1.0	Example 14	1.4
Example 15	1.4	Example 17	1.5
Example 18	0.3	Example 19	1.7
Example 20	0.7	Example 21	1.0
Example 22	1.0	Example 23	0.8
Example 24	1.1	Example 25	0.2
Example 26	0.5	Example 27	1.1
Example 28	0.7	Example 29	0.1
Example 30	0.6	Example 31	1.8
Example 32	0.8	Example 33	0.2
Example 34	0.3	Example 35	0.045
Example 36	3.3	Example 37	0.7
Example 38	2.3	Example 39	1.6
Example 41	0.2	Example 42	3.4
Example 43	0.2	Example 44	0.6
Example 45	1.8	Example 46	0.1
Example 47	1.1	Example 48	0.068
Example 49	0.07	Example 50	0.1
Example 51	0.1	Example 52	0.1
Example 53	0.05	Example 54	0.17
Example 55	0.048	Example 56	0.3
Example 57	0.2	Example 58	0.018

Table 1. (continued)

Compound	IC ₅₀ (μM)	Compound	IC ₅₀ (μM)
Example 59	0.055	Example 60	0.01
Example 61	0.6	Example 63	1.1
Example 64	0.5	Example 65	0.4
Example 66	0.5	Example 67	0.7
Example 68	0.05	Example 69	0.1
Example 70	0.14	Example 71	3.5
Example 72	9.2	Example 205	1.0
Example 216	1.4	Example 344	4.1
Example 355	22.1	Example 357	1.5
Example 371	2.9	Example 373	5.5
Example 388	0.8	Example 389	11.4
Example 390	6.3	Example 391	1.4
Example 392	5.3	Example 393	2.3
Example 394	6.4	Example 395	6.0
Example 396	4.4	Example 397	0.8
Example 398	1.9	Example 399	0.5
Example 400	6.0	Example 401	11.1
Example 402	9.3	Example 403	3.1
Example 404	1.76	Example 405	0.8
Example 406	36.2	Example 407	8.9
Example 408	5.4	Example 409	7.9
Example 410	8.7	Example 411	3.4
Example 412	2.5	Example 413	5.5
Example 414	1.5	Example 415	3.2
Example 416	0.7	Example 417	4.5
Example 418	2.6	Example 419	2.4
Example 420	1.3	Example 421	2.0
Example 422	2.6	Example 423	0.8

Table 1. (continued)

Compound	IC ₅₀ (μM)	Compound	IC ₅₀ (μM)
Example 424	2.9	Example 425	3.8
Example 426	3.5	Example 427	3.0
Example 428	2.3	Example 429	1.5
Example 430	3.3	Example 431	3.1
Example 432	2.0	Example 433	3.3
Example 434	7.6	Example 435	0.6
Example 436	1.4	Example 437	7.9
Example 438	4.4	Example 439	5.8
Example 440	2.8	Example 441	1.4
Example 442	2.1	Example 443	4.8
Example 444	1.9	Example 445	3.0
Example 446	1.0	Example 447	4.7
Example 448	3.2	Example 449	5.5
Example 450	3.3	Example 451	4.8
Example 452	7.3	Example 453	4.5
Example 454	5.0	Example 455	6.0
Example 456	6.6	Example 457	2.9
Example 458	3.8	Example 459	5.8
Example 460	10.5	Example 461	22.5
Example 462	8.9	Example 463	4.7
Example 464	22.6	Example 465	2.8
Example 466	8.3	Example 467	7.7
Example 468	23.3	Example 469	9.8
Example 470	4.6	Example 471	2.2
Example 472	3.7	Example 473	1.6
Example 474	1.7	Example 475	5.3
Example 476	6.5	Example 477	12.7
Example 478	3.4	Example 479	1.2
Example 480	2.8	Example 481	3.8

Table 1. (continued)

Compound	IC ₅₀ (μM)	Compound	IC ₅₀ (μM)
Example 482	0.7	Example 483	1.0
Example 484	1.2	Example 485	6.3
Example 486	2.5	Example 487	1.7
Example 488	6.4	Example 489	1.3
Example 490	16.2	Example 491	9.7
Example 492	10.3	Example 493	7.5
Example 494	4.0	Example 495	2.8
Example 496	8.9	Example 497	7.2
Example 498	3.3	Example 499	3.0
Example 500	3.9	Example 501	20.9
Example 502	5.3	Example 503	3.4
Example 504	1.3	Example 505	6.4
Example 506	3.6	Example 507	1.7
Example 508	0.9	Example 509	5.5
Example 510	5.7	Example 511	4.2
Example 512	3.3	Example 513	8.2
Example 514	4.8	Example 515	2.7
Example 516	3.0	Example 517	5.3
Example 518	11.7	Example 519	3.0
Example 520	6.6	Example 524	8.5
Example 526	0.2	Example 527	0.9
Example 528	0.3	Example 529	0.5
Example 530	0.3	Example 531	0.5
Example 532	0.5	Example 533	0.5
Example 534	1.5	Example 535	0.4
Example 536	0.6	Example 537	0.037
Example 539	1.7	Example 540	0.4
Example 541	3.2	Example 542	1.2
Example 543	1.6	Example 544	38.7

Table 1. (continued)

Compound	IC ₅₀ (μ M)	Compound	IC ₅₀ (μ M)
Example 545	0.1	Example 546	0.3
Example 547	0.4	Example 548	0.8
Example 549	0.7	Example 550	0.3
Example 551	0.3	Example 552	0.2
Example 553	1.1	Example 554	1.3
Example 555	0.9	Example 556	3.1
Example 557	0.4	Example 558	0.6
Example 559	0.5	Example 560	1.1
Example 561	1.1	Example 562	0.9
Example 563	1.3	Example 564	0.4
Example 565	0.5	Example 566	0.1
Example 567	0.1	Example 568	0.9
Example 569	2.2	Example 570	0.7
Example 571	2.7	Example 572	0.1
Example 573	0.3	Example 574	0.6
Example 575	0.02	Example 576	4.5
Example 577	11.4	Example 578	0.8
Example 579	1.5	Example 580	0.8
Example 581	0.07	Example 807	0.02
Example 808	0.13	Example 809	0.6
Example 810	0.9	Example 811	0.3
Example 812	0.6	Example 813	0.4
Example 814	0.9	Example 815	1.6
Example 816	0.6	Example 817	0.9
Example 818	0.4	Example 819	0.6
Example 820	0.1	Example 821	0.1
Example 822	0.1	Example 823	0.5
Example 824	2.5	Example 825	1.9

Table 1. (continued)

Compound	IC ₅₀ (μM)	Compound	IC ₅₀ (μM)
Example 826	6.2	Example 827	4.8
Example 828	3.0	Example 829	5.1
Example 830	2.7	Example 831	2.5
Example 832	0.6	Example 833	1.6
Example 834	0.1	Example 835	2.5
Example 836	0.2	Example 837	1.7
Example 838	11.0	Example 839	0.7
Example 840	1.6	Example 841	0.1
Example 842	1.3	Example 843	2.4
Example 844	0.4	Example 845	0.1
Example 846	2.9	Example 848	0.6
Example 849	1.0	Example 852	2.8
Example 854	33.0	Example 856	33.0
Example 857	24.2	Example 858	3.6
Example 859	4.4	Example 860	1.8
Example 861	4.1	Example 863	3.6
Example 864	3.4	Example 865	2.5
Example 866	1.2	Example 867	1.2
Example 868	0.1	Example 869	8.1
Example 871	0.8	Example 873	1.2

From results of Table 1, the compound of formula (I) according to the present invention were identified as having a potent inhibitory activity against K-ras transformed cell growth.

Experimental Example 2

In vitro inhibition of FPTase

Bovine brain cytosol was fractionated with ammonium sulfate and subjected the active fraction to ion exchange chromatography on a Mono Q column followed by gel filtration on sephacryl S-200. The Ras protein substrate, K-ras4B, is expressed in *Escherichia coli*. The donor of farnesyl residues to ras protein is [³H] farnesyl pyrophosphate (FPP). The standard reaction mixture contained the following concentrations of components in a final volume of 50 μ l ; 50 mM HEPES pH7.5, 5 mM MgCl₂, 5mM dithiothreitol (DTT), 10 μ M ZnCl₂, 0.2% n-Octyl- β -D-glucopyranoside and 300 nM K-ras4B. The mixture also contained 200 nM of [³H]FPP (16.0 Ci/mmol; Amersham Life Science) and 1.5 μ g of partially purified farnesyl-protein transferase.

Test compounds were dissolved in 99.9% ethyl alcohol (EtOH). After incubation for 1 hr at 37°C in 1.5 ml eppendorf tubes, the reaction was stopped by the addition of 90 μ l of 4% sodium dodecyl sulfate (SDS) and then 90 μ l of 30% trichloroacetic acid (TCA). The tubes were left on ice for 45-60 min and then the precipitates were transferred to Millipore multiscreen filtration 96-well plate with glass fiber C membrane (Millipore Corp.).

Following filtration using the multiscreen vacuum manifold, the wells were washed once with 200 μ l of 4%SDS/6%TCA and five times with 200 μ l of 6% TCA. Following removal of the bottom seal, excess washing fluid was blotted and the plates were allowed to dry before the filters were punched into 6 ml vials using the multiscreen punch. After punching, 5 ml of scintillation fluid (Packard) was added and radioactivity was determined by scintillation counting (Beckman LS5801). Dose-response curves for inhibitors used were duplicated at each drug concentration, and the IC₅₀ estimations were made from Litchfield-Wilcoxon method. The data presented below in Table 2 reflects the

ability of the test compound to inhibit ras farnesylation.

Table 2. *In vitro* inhibition of FPTase

Compound	IC ₅₀ (nM)	Compound	IC ₅₀ (nM)
Example 3.	60.2	Example 54.	17.3
Example 8.	188.1	Example 55.	11.2
Example 9.	44.8	Example 58.	1.7
Example 29.	30.8	Example 60.	3.7
Example 33.	7.8	Example 61.	21.4
Example 34.	115.4	Example 63.	28.3
Example 35.	26.7	Example 64.	2.6
Example 46.	2.9	Example 67.	11.6
Example 49.	5.6	Example 68.	5.4
Example 51.	20.4	Example 70.	1.4
Example 53.	7.0		
Example 418	805.1	Example 581	8.9
Example 419	714.7	Example 807	24.5
Example 420	573.2	Example 808	28.0
Example 422	390.1	Example 813	69.7
Example 423	354.7	Example 815	6.9
Example 424	963.8	Example 817	228.7
Example 425	690.6	Example 820	35.3
Example 428	405.8	Example 822	39.3
Example 432	70.0	Example 832	906.0
Example 452	54.6	Example 834	44.2
Example 526	85.6	Example 837	162.8
Example 529	49.0	Example 839	107.1
Example 530	54.6	Example 858	254.9
Example 532	3.0	Example 859	229.2
Example 533	27.9	Example 862	250.8
Example 537	15.4	Example 863	89.5

From results of Table 2, the formula (I) of this invention were

identified as having an ability to inhibit FPTase effectively.

Experimental Example 3

Inhibition of K-ras4B processing

NIH3T3 cells transfected with oncogenic human K-ras4B were plated in 6-well plate and cultured until 10^5 per well. The cells were treated for 48 hours with either vehicle or the test compounds (each $10\ \mu\text{M}$). Cells were washed and lysed in 1 ml of lysis buffer ($1\times$ PBS(phosphate buffer saline), 1% Triton X-100, 1 mM phenylmethylsulfonyl fluoride, $25\ \mu\text{g/ml}$ leupeptin, $16\ \mu\text{g/ml}$ benzamidine HCl, 1 mg/ml Sigma-104 phosphate substrate) at 4°C for 1 hour. Lysates were cleared (10,000 rpm, 4°C , 15 min), and equal amounts of protein were immunoprecipitated with the anti-ras antibody-agarose beads (OP01A, Oncogene Science) at 4°C for 2 hours. The immunoprecipitated proteins were separated on a 15% SDS-PAGE, transferred to Hybond-ECL (Amersham Corp.), and immunoblotted using an anti-K-ras antibody (OP24, Oncogene Science). Antibody reactions were visualized using peroxidase-conjugated goat anti-mouse IgG and an enhanced chemiluminescence detection system (ECL, Amersham Corp.).

Posttranslational modifications have different effects on electrophoretic mobility. Unprocessed ras protein migrate slightly faster than their prenylated counterparts. Therefore, the intensities of the bands corresponding to prenylated and nonprenylated K-ras proteins were compared to determine the inhibition of prenyl transfer to protein. The results of effective compounds presented in Table 3 reflects the ability to inhibit K-ras4B processing.

Table 3. Inhibition of K-ras4B processing by compounds of this invention.

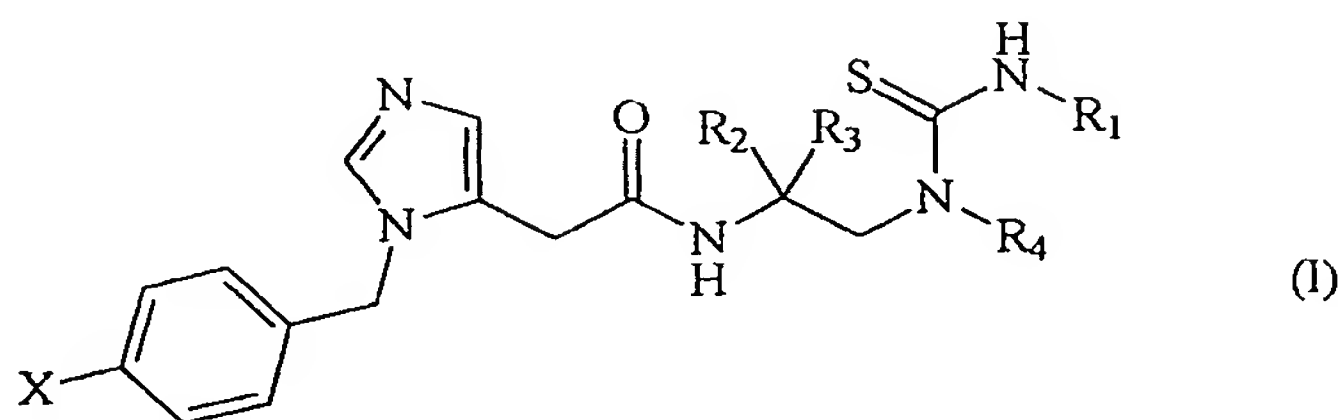
Compound	Inhibitory effect	Compound	Inhibitory effect
Example 21.	-	Example 54.	+
Example 25.	+	Example 60.	+++
Example 33.	++	Example 61.	++
Example 34.	+	Example 64.	+
Example 35.	+++	Example 67.	+
Example 46.	+++	Example 68.	+++
Example 48.	++	Example 70.	+++
Example 53.	++		

The sign '-' indicates no effect; and '+' to '+++' indicates increasing inhibition of K-ras4B processing. Inhibitory effect; '+++': 80~100%, '++': 40~80%, '+': 10~40%, '-': < 10%.

From the results of Table 3, the compound of formula (I) according to the present invention were identified as having an ability to inhibit K-ras4B processing effectively.

WHAT IS CLAIMED IS:

1. A thiourea derivative represented by the following formula (I):



pharmaceutically acceptable salt or stereoisomer thereof, wherein

- R_1 represents hydrogen; straight-chain or branched C_1 - C_8 -alkyl which is optionally substituted by substituents selected from a group consisting of halogen, C_1 - C_6 -alkoxy, C_1 - C_6 -alkoxycarbonyl and di(C_1 - C_4 -alkyl)amino; C_2 - C_6 -alkenyl; C_1 - C_4 -alkoxycarbonyl; C_3 - C_6 -cycloalkyl; phenyl which is optionally mono- to trisubstituted by substituents selected from a group consisting of halogen, C_1 - C_6 -alkyl, C_1 - C_6 -alkoxy, C_1 - C_6 -alkylthio, halogeno- C_1 - C_6 -alkyl, azido, nitro, amino, phenyl, di(C_1 - C_4 -alkyl)amino and hydroxy; phenyl- C_1 - C_4 -alkyl; naphthyl which is optionally substituted by di(C_1 - C_4 -alkyl)amino; benzoyl; pyridyl which is optionally substituted by substituents selected from a group consisting of halogen and C_1 - C_6 -alkoxy; or adamantyl,
- R_2 and R_3 independently of one another represent hydrogen, straight-chain or branched C_1 - C_6 -alkyl, C_3 - C_6 -cycloalkyl or benzyloxy-benzyl,

R₄ represents C₁-C₄-alkyl substituted by phenyl wherein the phenyl moiety is optionally mono- to trisubstituted by substituents selected from a group consisting of halogen, halogeno-C₁-C₄-alkyl, C₁-C₄-alkylenedioxy, C₁-C₆-alkyl, nitro, C₁-C₆-alkoxy, carboxyl and C₁-C₆-alkoxycarbonyl; naphthyl-C₁-C₄-alkyl; thiophenyl-C₁-C₄-alkyl; C₁-C₆-alkyl which is optionally substituted by substituents selected from a group consisting of pyridyl, oxypyridyl, C₁-C₆-alkoxy and C₁-C₆-alkylthio; or C₂-C₆-alkynyl, and

X represents nitro or cyano.

2. The compound of claim 1, wherein

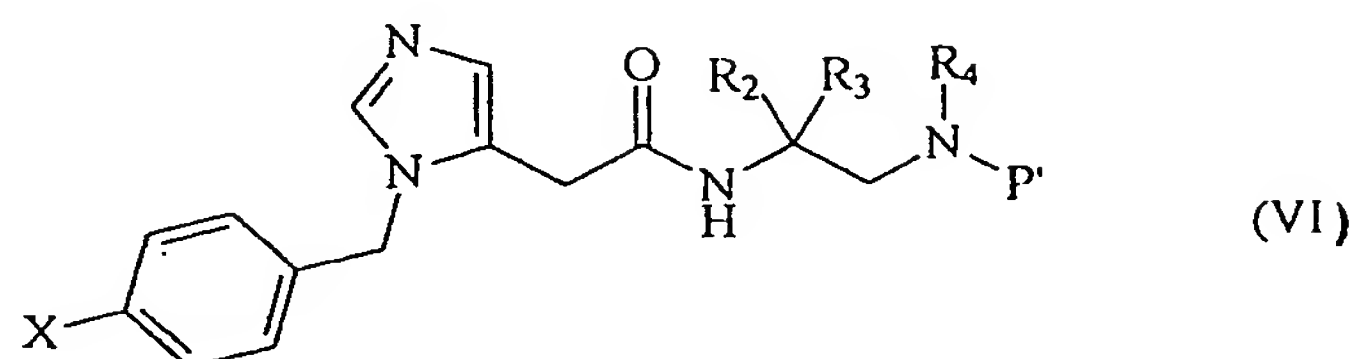
R₁ represents phenyl which is optionally mono- to trisubstituted by substituents selected from a group consisting of halogen, C₁-C₆-alkyl, C₁-C₆-alkoxy, C₁-C₆-alkylthio, halogeno-C₁-C₆-alkyl, azido, nitro, amino, phenyl, di(C₁-C₄-alkyl)amino and hydroxy; or pyridyl which is optionally substituted by substituents selected from a group consisting of halogen and C₁-C₆-alkoxy,

R₂ and R₃ independently of one another represent straight-chain or branched C₁-C₆-alkyl,

R₄ represents C₁-C₄-alkyl substituted by phenyl wherein the phenyl moiety is optionally mono- to trisubstituted by substituents selected from a group consisting of halogen, halogeno-C₁-C₄-alkyl, C₁-C₄-alkylenedioxy, C₁-C₆-alkyl, nitro, C₁-C₆-alkoxy, carboxyl and C₁-C₆-alkoxycarbonyl; and

X represents nitro or cyano.

3. A process for preparing a thiourea derivative of formula (I) as defined in claim 1, characterized in that a compound represented by the following formula (VI):

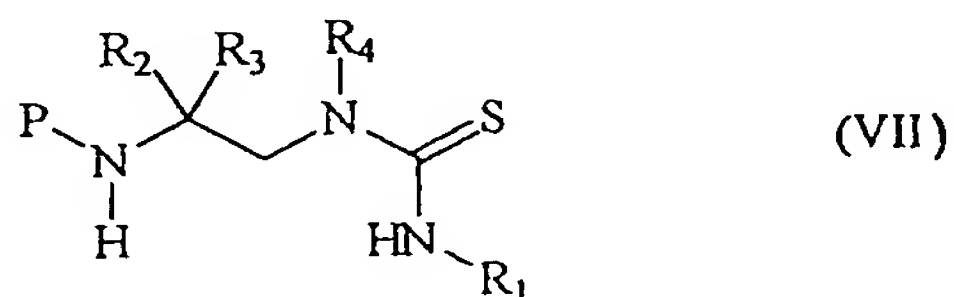


wherein R_2 , R_3 , R_4 and X are defined in claim 1 and P' represents an amino-protecting group, is deprotected and then reacted with a substituted isothiocyanate represented by the following formula (VIII):



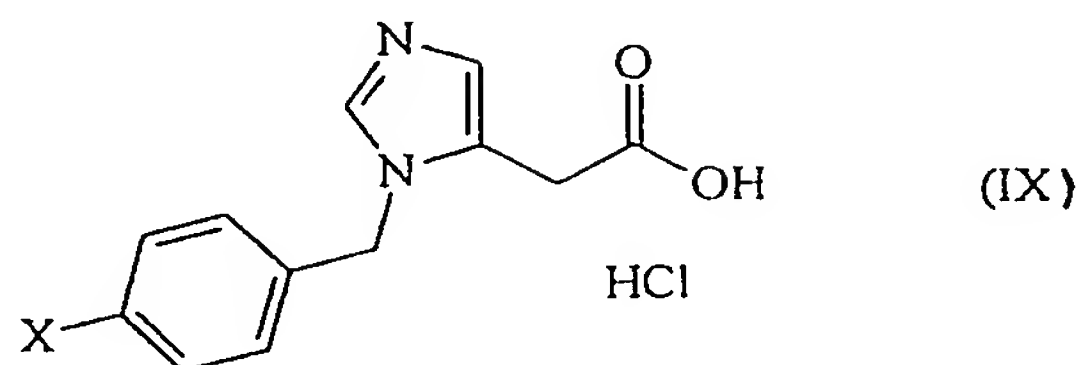
wherein R_1 is defined in claim 1, if appropriate, in an organic solvent.

4. A process for preparing a thiourea derivative of formula (I) as defined in claim 1, characterized in that a compound represented by the following formula (VII):



wherein R_1 , R_2 , R_3 and R_4 are defined in claim 1 and P represents an amino-protecting group, is deprotected and then reacted with a

1-substituted-1H-imidazol-5ylacetic acid hydrochloride represented by the following formula (IX):



wherein X is defined in claim 1, if appropriate, in the presence of a coupling agent.

5. A pharmaceutical composition for inhibition of ras-transformed cell growth comprising a therapeutically effective amount of the compound of formula (I), as defined in claim 1, or a pharmaceutically acceptable salt thereof as an active ingredient together with a pharmaceutically acceptable carrier.

INTERNATIONAL SEARCH REPORT

Intern: application No.

PCT/KR 98/00268

A. CLASSIFICATION OF SUBJECT MATTER

IPC⁶: C 07 D 233/64, A 61 K 31/415

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC⁶: C 07 D 233/64, A 61 K 415

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

DARC, CAS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 91/16 340 (BOARD OF REGENTS THE UNIVERSITY OF TEXAS SYSTEM) 31 October 1991 (31.10.91), abstract. -----	1-5

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

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Date of the actual completion of the international search

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Disclosed are methods and compositions for the identification, characterization and inhibition of farnesyl protein transferase, enzymes involved in the farnesylation of various cellular proteins, including cancer related *ras* proteins such as p21^{ras} one farnesyl protein transferase which is disclosed herein exhibits a molecular weight of between about 70,000 and about 100,000 upon gel exclusion chromatography. The enzyme appears to comprise one or two subunits of approximately 50 kDa each. Methods are disclosed for assay and purification of the enzyme, as well as procedures for using the purified enzyme in screening protocols for the identification of possible anticancer agents which inhibit the enzyme and thereby prevent expression of proteins such as p21^{ras}. Also disclosed is a family compound which act either as false substrates for the enzyme or as pure inhibitors and can therefore be employed for inhibition of the enzyme. The most potent inhibitors are ones in which phenylalanine occurs at the third position of a tetrapeptide whose amino terminus is cysteine.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/KR 98/00268

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